UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF PENNSYLVANIA

DR. WILLIAM TOMASZEWSKI, individually and on behalf of all others similarly situated, Plaintiff, v. TREVENA, INC., MAXINE GOWEN, and DAVID SOERGEL, Defendants.	Case No. 2:18-cv-04378 (consolidated with 2:18-cv-04426) **First Consolidated and Amended Class Action Complaint for Violations of the Federal Securities Laws** ***Jury Trial Demanded***

Lead Plaintiffs Albert Koch, Whittier Pierce, Christopher Beyers, Kevin Walsh, and Peter Palmer (together "Lead Plaintiffs"), by and through their attorneys, allege upon personal knowledge as to themselves individually, and upon information and belief as to all other matters, based upon the investigation conducted by and through their attorneys, which included, among other things, a review of documents filed by Defendants (as defined below) with the United States Securities and Exchange Commission ("SEC"), the United States Food and Drug Administration ("FDA"), news reports, press releases issued by Defendants, transcripts of earnings calls and investor conferences attended by Defendants, and other publicly available documents, as follows:

NATURE AND SUMMARY OF THE ACTION

1. This is a securities fraud action against Trevena, Inc. ("Trevena" or the "Company"), its former Chief Executive Officer, Maxine Gowen, and its former Chief Medical Officer David Soergel. This action charges that between May 2, 2016 and October 9, 2018, inclusive (the "Class Period"), Defendants materially misrepresented and omitted to disclose material facts about the Company's interactions with the FDA concerning its leading drug candidate, oliceridine.

2. Trevena is a clinical-stage biopharmaceutical company headquartered in Chesterbrook, Pennsylvania. Throughout the Class Period, Trevena's leading drug candidate was Olinvo (also known as "TRV-130" or "oliceridine"), which the Company described as a "G protein-based ligand binding to the mu opioid receptor for the intravenous treatment of acute moderate-to-severe postoperative pain." The Company promoted Olinvo as a potential replacement for morphine.

3. On March 29, 2016, Trevena attended an end-of-phase-two-trial meeting with the FDA about oliceridine, in order to discuss Trevena's proposed Phase 3 studies. At the meeting, the FDA staff advised Trevena that the FDA "did not agree with the proposed dosing in the Phase 3 studies," "did not agree with [Trevena's] proposed primary endpoint" of its Phase 3 study, and "did not agree with the proposed non-inferiority (NI) margin for comparing morphine to oliceridine" that Trevena was proposing to conduct its Phase 3 trials.

4. The FDA makes clear through policy documents that any attendee of a meeting with the agency should leave with a clear understanding of what occurred at the meeting. To facilitate that understanding, minutes of meetings are prepared and sent to meeting attendees. Here, Trevena received a copy of the FDA's minutes from the March 29, 2016 meeting on April 28, 2016, clearly setting out the FDA's concerns with Trevena's proposed Phase 3 study.

5. Despite knowing of the FDA's concerns and criticisms of Trevena's proposed Phase 3 study, Defendants knowingly, or in reckless disregard for the truth, misrepresented what transpired at the March 29, 2016 meeting and omitted to disclose material facts necessary to make the statements that were made not misleading. On May 2, 2016, the Company announced that it had concluded a "Successful End-of-Phase 2 Meeting with FDA," where the Company "reached general agreement with the FDA on key elements of the Phase 3 program to support a New Drug

Application (NDA) for olicerdine (TRV130).” Although Defendant Gowen informed investors that Trevena was “very pleased with the outcome” of the meeting, she omitted to disclose the material facts that the FDA disagreed with Trevena’s proposals regarding key measures of the Phase 3 study.

6. The FDA has a longstanding policy of keeping confidential its interactions with drug developers during clinical trials, only releasing information close to the time it decides whether to grant or deny approval to a new drug. This policy is in place even when a drug company directly misrepresents its interactions with the agency to the public, as happened here.

7. By misrepresenting the FDA’s disagreements with Trevena’s proposed Phase 3 trial measurements, Defendants misrepresented, and omitted to disclose material facts, concerning Olinvo’s prospects for FDA approval.

8. Trevena continued to misrepresent its interactions with the FDA to the public for two years, all while it continued to meet with the agency, and continued to receive negative feedback about how its Phase 3 trials were proceeding.

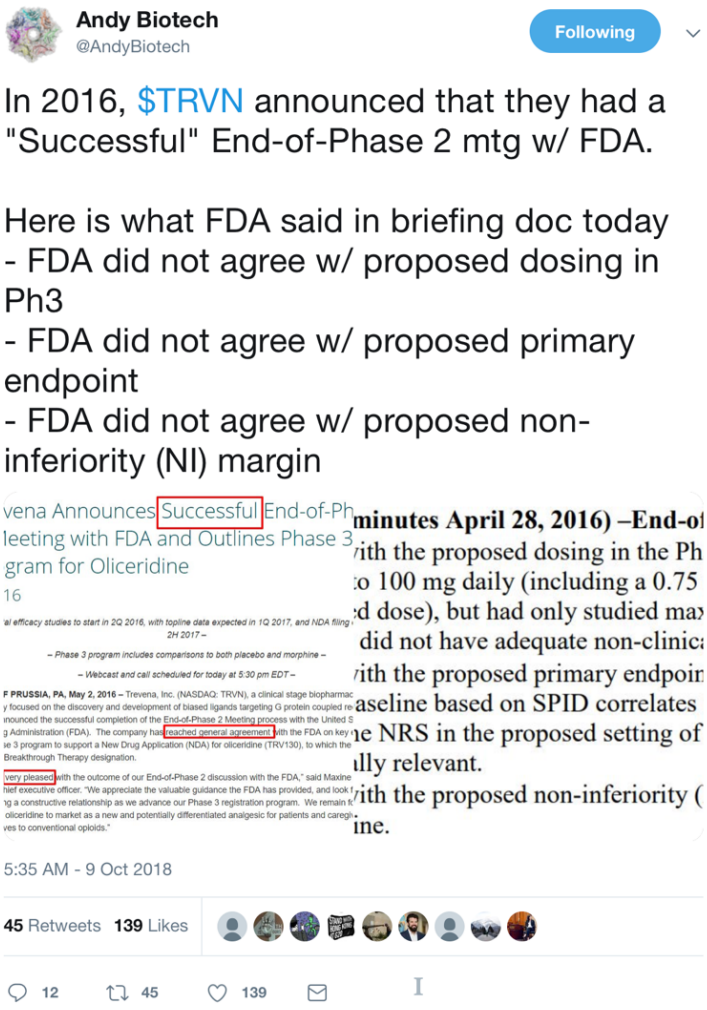
9. The jig was up for Trevena on October 9, 2018. That morning, as is its policy, the FDA’s Anesthetic and Analgesic Drug Products Advisory Committee issued its Briefing Document in advance of its previously scheduled October 11, 2018 meeting to vote on its recommendation to the FDA concerning the approval of olicerdine.[1] Investors immediately knew

[1] Prior to making a final decision concerning approval of a particular application, the FDA will often designate an advisory committee to hold a meeting regarding the application and make a recommendation to the FDA. According to the FDA’s website: “Advisory committees provide FDA with independent advice from outside experts on issues related to human and veterinary drugs, vaccines and other biological products, medical devices, and food. In general, advisory committees include a chair, several members, plus a consumer, industry, and sometimes a patient representative. Additional experts with special knowledge may be added for individual committee meetings as needed. Although the committees provide advice to the agency, FDA makes the final decisions.” *See* https://www.fda.gov/about-fda/fda-basics/what-fda-advisory-committee.

the concealed information did not bode well for FDA approval as FDA staff disagreed with Trevena's key elements of its phase 3 studies.

10. The release of the Briefing Document revealed for the first time to the public what Trevena knew and hid for years: the FDA did not agree with Trevena's proposed dosing in Phase 3, did not agree with its proposed primary endpoint, and did not agree with its proposed non-inferiority margin.

11. Trevena shares fell over 64% on the news, while analysts and observers quickly acknowledged that the Company had been lying and had lost all credibility:



12. Stock market analysts, who closely followed Trevena, were similarly shocked. Biren Amin, from Jefferies, stated in reaction to the news "***To our surprise,*** TRVN proposed endpoint for assessing respiratory safety burden ***was not supported by the FDA, and this information was not disclosed to the public following the end-of-phase 2 FDA meeting.***"

13. Trevena stock crumbled: it traded at $2.98 per share on October 8, 2018 but fell to $1.07 per share at closing on October 9, 2018. This was a drop of 64%, representing a loss in market capitalization of over $157 million.

14. This action seeks to recover damages on behalf of investors that purchased their shares during the time period that Trevena's common stock was artificially inflated due to Defendants' misrepresenting material facts, and omitting to disclose material facts necessary to not make the statements it made not misleading, concerning key interactions with the FDA, including the March 29, 2016 End-of-Phase 2 meeting.

JURISDICTION AND VENUE

15. This Court has jurisdiction over this action under Section 27 of the Exchange Act, 15 U.S.C. § 78aa. The claims asserted herein arise under Sections 10(b) and 20(a) of the Exchange Act, 15 U.S.C. §§ 78j(b) and 78t(a), *et seq.*, and Rule 10b-5 promulgated thereunder, 17 C.F.R. § 240.10b-5. The Court also has subject matter jurisdiction under 28 U.S.C. § 1331.

16. Venue is proper in the Eastern District of Pennsylvania under 28 U.S.C. § 1391(b) and under Section 27 of the Exchange Act, 15 U.S.C. § 78aa, because Trevena is located in this district and most of the false and misleading statements alleged herein were disseminated from this District.

17. Defendants used the means and instrumentalities of interstate commerce, either directly or indirectly, including, but not limited to, the mails, interstate telephone communications, the internet, and the facilities of the national securities markets, in connection with the acts alleged in this Complaint.

PARTIES

18. Defendant Trevena is a development-stage biopharmaceutical company. On May 8, 2019, the Company reported that there were 92,353,638 shares of Trevena common stock outstanding. Those shares trade in an efficient market, on the NASDAQ exchange, under the ticker symbol TRVN.

19. Defendant Maxine Gowen was the Chief Executive Officer of Trevena from the beginning of the Class Period until she announced that she was retiring on April 4, 2018, effective on or about October 1, 2018.

20. Defendant David Soergel was the Chief Medical Officer of Trevena from the beginning of the Class Period until he announced he was resigning in July 2017.

21. Defendants Gowen and Soergel are referred to herein either by their last name or together as the "Individual Defendants". References to "Defendants" are to all of the Individual Defendants plus Trevena.

22. Lead Plaintiff Christopher Beyers is a Minneapolis, Minnesota resident whose Class Period transactions in Trevena Stock are reflected in his previously filed certification (ECF No. 8-4).

23. Lead Plaintiff Albert Koch is a resident of Alberta, Canada whose Class Period transactions in Trevena Stock are reflected in his previously filed certification (ECF No. 8-5).

24. Lead Plaintiff Peter Palmer is a Belmont, New Hampshire resident whose Class Period transactions in Trevena Stock are reflected in his previously filed certification (ECF No. 8-6).

25. Lead Plaintiff Whittier Pierce is a Danbury, Connecticut resident whose Class Period transactions in Trevena Stock are reflected in his previously filed certification (ECF No. 8-7).

26. Lead Plaintiff Kevin Walsh is a North Myrtle Beach, South Carolina resident whose Class Period transactions in Trevena Stock are reflected in his previously filed certification (ECF No. 8-8).

FACTUAL ALLEGATIONS

PRE-CLASS PERIOD DEVELOPMENTS

27. Trevena is a clinical-stage biopharmaceutical company with headquarters in Chesterbrook, Pennsylvania.

28. At the start of the Class Period, Trevena's leading drug candidate was Olinvo (also known as "TRV130" or "oliceridine"), which it described as a "G protein-based ligand binding to

the mu opioid receptor for the intravenous treatment of acute moderate-to-severe postoperative pain."

29. When the Company announced the results of its Phase 2b study in a press release on August 31, 2015, it described that Olinvo "when given on-demand, matched morphine efficacy for pain relief with a markedly improved safety and tolerability profile." In other words, Trevena was claiming that Olinvo was as effective as morphine, but with reduced side effects such as "reduced nausea, vomiting, and hypoventilation events."

30. The study's lead investigator said that the data in the Phase 2 study "suggested that, if approved, [Olinvo] may provide a better option than currently available opioid analgesics."

31. Defendant Gowen said in the August 31, 2015 press release: "[t]he positive data from this study continue the impressive accumulation of evidence suggesting meaningful differentiation of TRV130 from morphine. The goal of new analgesic drug discovery has long been the provision of more powerful pain relief with reduced opioid-related adverse effects. We believe the Trevena biased ligand platform has delivered this profile in TRV130 and we look forward to starting Phase 3 development in early 2016."

32. On January 19, 2016, the Company issued a press release entitled *Trevena, Inc. Announces Initiation of Oliceridine Phase 3 Clinical Program*. The press release noted that the Company's "End-of-Phase 2 meeting with the FDA" was "scheduled for later this quarter." Defendant Gowen stated "we also look forward to discussing the oliceridine Phase 3 program with the FDA later this quarter and remain on track to file a [New Drug Application] for oliceridine in the second half of 2017."

33. On March 3, 2016, the FDA issued private, non-public written advice to Trevena, asking the Company to "submit amendments to modify all protocols for ongoing clinical trials" to

include certain safety assessments, because Trevena's current study saw "QTcF prolongation [which] exceeded the 10-ms regulatory threshold at clinically relevant exposures." The FDA asked Trevena to:

> 1. Conduct safety ECG monitoring at baseline, following the first dose, and periodically thereafter. The timing of ECGs will need to reflect the delayed response relative to time of peak concentrations that was observed in the thorough QT study. Include additional ECG monitoring until ECGs return to baseline in patients discontinued from the trial or requiring dose reduction due to QTc interval prolongation.
>
> 2. Periodic monitoring of electrolytes (subjects already participating in the study with serum potassium, magnesium, or calcium levels outside of the central laboratory's reference range should be carefully monitored and brought to normal values).
>
> 3. Propose dose-modification and discontinuation criteria in subjects with posttreatment QTc > 500 ms or post-baseline increases > 60 ms.

34. On March 29, 2016, Trevena executives met in private with the FDA for the End-of-Phase 2 Meeting.

35. The End-of-Phase 2 Meeting did not go well for Trevena. The FDA told the Company during the meeting that it:

a. Did not agree with the Company's proposed dosing in its Phase 3 studies. Trevena had proposed 100mg of daily dosing, but had only studies doses up to 36.8 mg. Further, the FDA informed Trevena that it did not have adequate non-clinical support for its proposed 100mg doses.

b. Did not agree with Trevena's proposed primary endpoint for its Phase 3 study. The FDA said that it was "unclear how a 30% improvement from baseline based on SPID correlates to an improvement in pain intensity scores on the NRS in the

proposed setting of acute postoperative pain and if that change is clinically relevant."

c. Did not agree with Trevena's proposed non-inferiority (NI) margin for comparing morphine to oliceridine.

36. The FDA also informed Trevena that its safety database must include "at least 350 patients exposed to the highest intended dose for the longest expected duration of use." The FDA told Trevena that "safety database requirements might change if safety signals arise during development that require further evaluation."

37. The FDA also warned that "comparative safety claims must be replicated, adequately justified for clinical relevance, and established in the setting of comparable efficacy between comparators to be considered for inclusion in labeling."

38. Trevena executives who attended the FDA meeting should have left that meeting understanding precisely the what the FDA's concerns were about Trevena's Phase 3 studies, including that the FDA did not agree with the Company's dosing proposal, proposed primary endpoint, or proposed non-inferiority margin. And, since the FDA warned that any comparative safety claims had to be "established in the setting of comparable efficacy between comparators to be considered for inclusion in labeling," Trevena had significantly diminished prospects of securing such claims given that the FDA did not agree with its method for comparing oliceridine to morphine.

39. As the oldest consumer protection agency in the United States, the FDA is charged with ensuring that drugs in the marketplace are both safe and effective. To that end, the FDA may approve a drug for market only where there is (a) sufficient information to determine the drug is safe to use as proposed, and (b) substantial evidence the drug will have the effect it is purported to

have when used as proposed. 21 U.S.C. § 355(d)(4)(5).[2] According to the FDA: "At the end of Phase 2, the FDA and sponsors try to come to an agreement on how large-scale studies in Phase 3 should be done. . . . These studies gather more information about safety and effectiveness, studying different populations at different dosages and using the drug in combination with other drugs."[3] Concerning Phase 3 studies, the FDA provides:

> **Purpose**: Efficacy and monitoring of adverse reactions
>
> Researchers design Phase 3 studies to demonstrate whether or not a product offers a treatment benefit to a specific population. Sometimes known as pivotal studies, these studies involve 300 to 3,000 patients.
>
> Phase 3 studies provide most of the safety data. In previous studies, it is possible that less common side effects might have gone undetected. Because these studies are larger and longer in duration, the results are more likely to show long-term or rare side effects.[4]

40. The FDA publishes a document entitled *Guidance for Industry: Formal Meetings Between the FDA and Sponsors or Applicants*. The version of this document in effect at the time of this meeting stated clearly:

> Before the end of the meeting, FDA attendees and the requested attendees should summarize the important discussion points, agreements, clarifications, and action items. Generally, the requester will be asked to present the summary to ensure that there is mutual understanding of meeting outcomes and actions. FDA staff can add or further clarify any important points not covered in the summary and those items can be added to the meeting minutes.

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[2] *See also Frequently Asked Questions about the FDA Approval Process*, (Q: "Why are drugs evaluated by the FDA?" A: "Drugs intended for human use are evaluated by the FDA[] . . . to ensure that drugs marketed in the United States are **safe** and **effective**.") *available at*: https://www.fda.gov/drugs/special-features/frequently-asked-questions-about-fda-drug-approval-process (last visited July 29, 2019).

[3] https://www.fda.gov/drugs/drug-information-consumers/fdas-drug-review-process-ensuring-drugs-are-safe-and-effective.

[4] https://www.fda.gov/patients/drug-development-process/step-3-clinical-research.

41. If there were any doubt at all about the FDA's concerns, those doubts were erased when the agency sent written minutes to Trevena from this meeting on April 28, 2016. These written minutes, which were shared only with Trevena, made clear:

> FDA did not agree with the proposed dosing in the Phase 3 studies. The Sponsor proposed dosing up to 100 mg daily (including a 0.75 mg every 1 hour as needed clinician administered dose), but had only studied maximum daily doses of 36.8 mg. Further, the Sponsor did not have adequate non- clinical support for the proposed doses.
>
> FDA did not agree with the proposed primary endpoint, as it was unclear how a 30% improvement from baseline based on SPID correlates to an improvement in pain intensity scores on the NRS in the proposed setting of acute postoperative pain and if that change is clinically relevant.
>
> FDA did not agree with the proposed non-inferiority (NI) margin for comparing morphine to oliceridine.
>
> FDA noted that the safety database must include at least 350 patients exposed to the highest intended dose for the longest expected duration of use. It was noted that the safety database requirements might change if safety signals arise during development that require further evaluation.
>
> Any comparative safety claims must be replicated, adequately justified for clinical relevance, and established in the setting of comparable efficacy between comparators to be considered for inclusion in labeling[.]
>
> The Applicant provided details of a proposed approach to missing data. This approach included replacing pain scores in the window determined dosing interval described in the label of the rescue medication following rescue with the pain score recorded immediately prior to rescue.

THE CLASS PERIOD BEGINS
TREVENA STARTS LYING TO THE PUBLIC

42. Knowing all of the above, on May 2, 2016, Trevena issued a press release entitled *Trevena Announces Successful End-of-Phase 2 Meeting with FDA and Outlines Phase 3 Program for Oliceridine.*

43. The press release stated as follows:

Trevena Announces Successful End-of-Phase 2 Meeting with FDA and Outlines Phase 3 Program for Oliceridine

— Pivotal efficacy studies to start in 2Q 2016, with topline data expected in 1Q 2017, and NDA filing expected in 2H 2017 —

— Phase 3 program includes comparisons to both placebo and morphine —

— Webcast and call scheduled for today at 5:30 pm EDT —

KING OF PRUSSIA, PA, May 2, 2016 — Trevena, Inc. (NASDAQ: TRVN), a clinical stage biopharmaceutical company focused on the discovery and development of biased ligands targeting G protein coupled receptors, today announced the ***successful completion of the End-of-Phase 2 Meeting process*** with the United States Food and Drug Administration (FDA). The company has reached ***general agreement with the FDA on key elements of the Phase 3 program*** to support a New Drug Application (NDA) for oliceridine (TRV130), to which the FDA has granted Breakthrough Therapy designation.

"We are ***very pleased with the outcome of our End-of-Phase 2 discussion with the FDA***," said Maxine Gowen, Ph.D., chief executive officer. "We appreciate the valuable guidance the FDA has provided, and look forward to continuing a constructive relationship as we advance our Phase 3 registration program. We remain focused on bringing oliceridine to market as a new and potentially differentiated analgesic for patients and caregivers seeking alternatives to conventional opioids."

End-of-Phase 2 meeting

The FDA agreed that pivotal efficacy trials in bunionectomy and abdominoplasty patients include appropriate patient populations to support an indication for moderate to severe acute pain. The agency also confirmed the need for at least 1,100 patients exposed to oliceridine across the development program for the purposes of evaluating safety and tolerability. This database should include a sufficient number of patients with higher exposures and longer durations of oliceridine therapy. In addition, general agreement was reached on the company's planned clinical, nonclinical, clinical pharmacology, and chemistry, manufacturing and control (CMC) activities to support the planned NDA.

Overview of the Oliceridine Phase 3 program

The oliceridine Phase 3 program includes two pivotal efficacy trials evaluating moderate-to-severe acute pain: the APOLLO-1 study will evaluate pain for 48 hours following bunionectomy, and the APOLLO-2 study will evaluate pain for 24 hours following abdominoplasty. In each trial, patients will be randomized to receive placebo, morphine, or one of three regimens of oliceridine by patient-controlled analgesia (PCA) for the management of their post-operative pain. Each study will enroll approximately 375 patients, allocated equally across study arms.

The primary endpoint for both APOLLO studies will be a responder analysis proposed by the company comparing active treatment arms to placebo. A responder is defined as a patient experiencing a sum of pain intensity difference (SPID) at the end of the treatment period that corresponds to at least a 30% improvement from baseline without early discontinuation and without rescue pain medication.

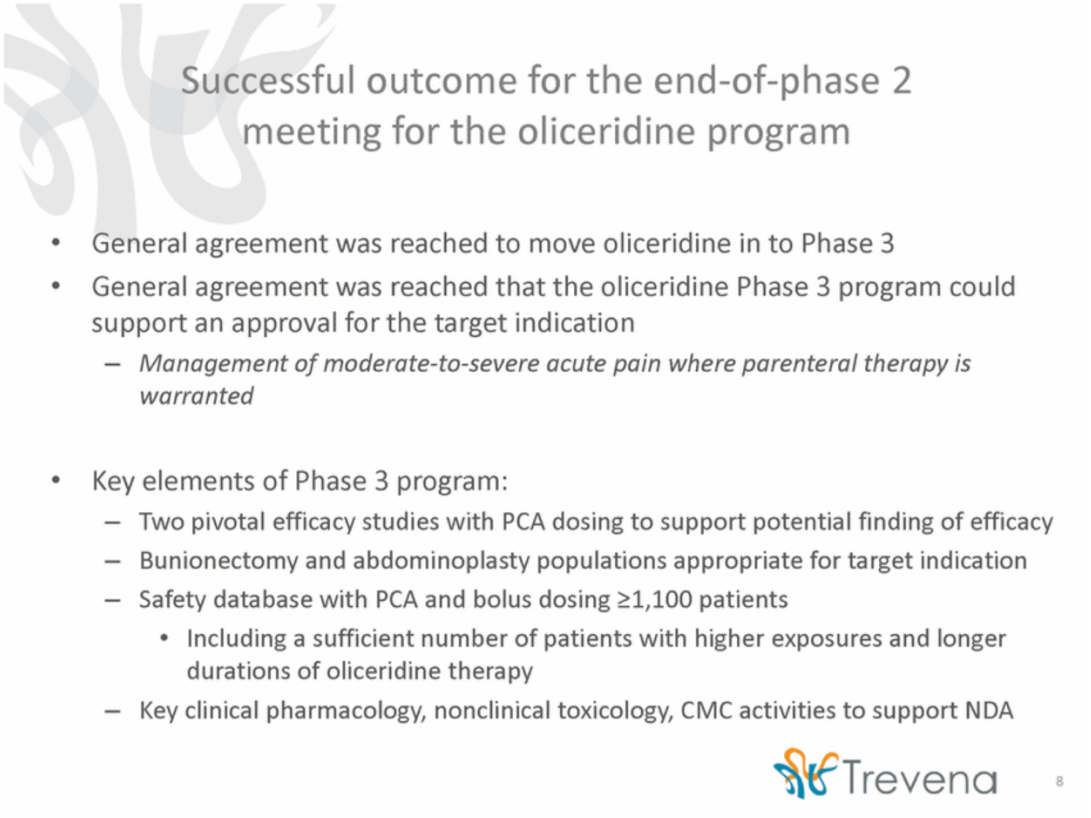
Secondary endpoints in both APOLLO studies will include comparisons of oliceridine efficacy, safety, and tolerability to morphine. A respiratory safety endpoint will measure prevalence and duration of hypoventilation, which will be a clinical assessment as in the company's Phase 2b abdominoplasty study.

The APOLLO study designs were informed in part by the company's Phase 2b abdominoplasty study, which also used PCA dosing. Powering assumptions included similar performance of PCA-administered oliceridine in both APOLLO studies as was observed in the Phase 2b study. In a post-hoc evaluation using the Phase 3 responder analysis, both doses in the company's Phase 2b study in abdominoplasty yielded analgesic efficacy similar to morphine, and significantly higher than placebo ($p < 0.0005$ for both oliceridine treatment arms). In addition, using the Phase 3 respiratory safety endpoint, both doses in the company's Phase 2b study showed significantly less respiratory safety burden for oliceridine than morphine ($p < 0.0003$ for both oliceridine treatment arms).

The development program will include at least 1,100 patients exposed to oliceridine. The on-going open-label ATHENA-1 safety study is enrolling patients experiencing pain as a result of either a medical diagnosis or surgery. In this study, patients may receive

> oliceridine as-needed either as an intermittent bolus or via PCA device, with doses and durations appropriate to manage their pain.
>
> Both APOLLO-1 and APOLLO-2 are expected to start in the second quarter of this year, and the company expects to report top-line data in the first quarter of 2017. The company continues to expect to file an NDA for oliceridine in the second half of 2017. The company also continues to expect that its available cash and investments will be sufficient to fund operations into 2018.

44. On the same day, Trevena made an investor presentation, which included the following slides:



Pivotal efficacy studies to support potential approval

- Two pivotal studies: same surgical models as in Phase 2
  - APOLLO-1: 48 hour treatment following bunionectomy
  - APOLLO-2: 24 hour treatment following abdominoplasty
  - Each study will include 375 patients, 75/group
- Primary endpoint: efficacy of oliceridine vs. placebo
- Secondary endpoints: oliceridine vs. morphine
  - Efficacy, including pain intensity difference and time to onset
  - Safety, including respiratory safety burden based on hypoventilation events
  - Tolerability, including nausea and vomiting

Trevena 10

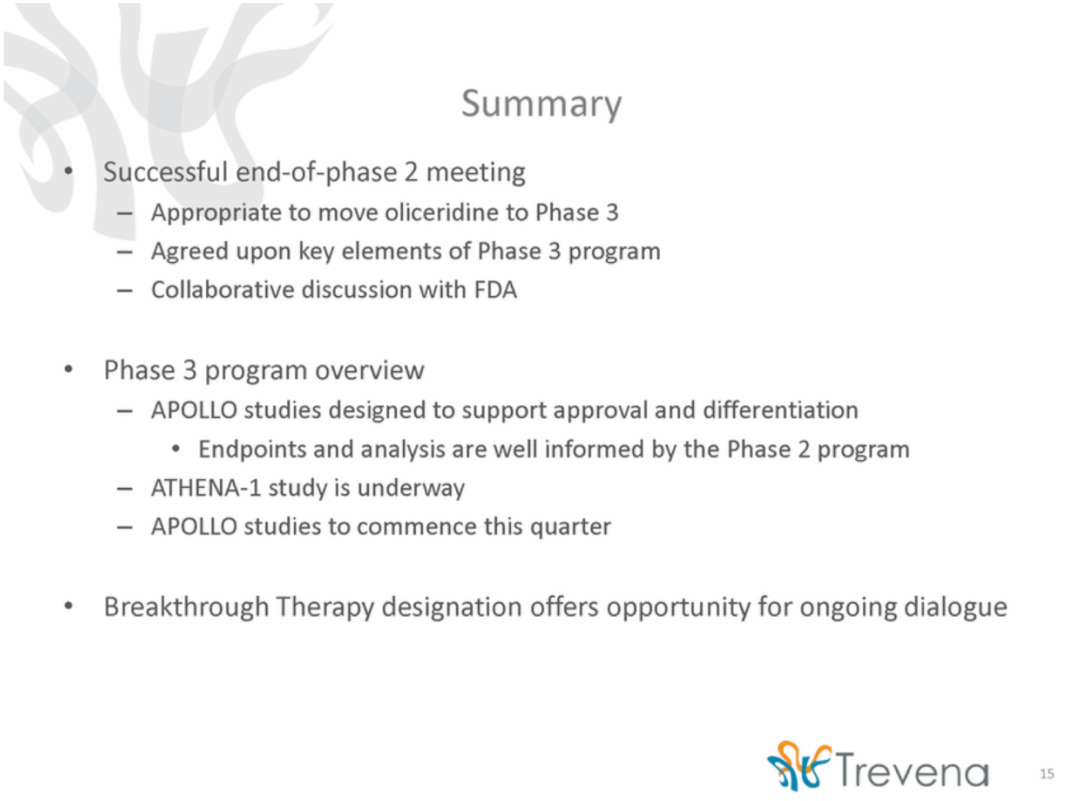
Pivotal efficacy studies: primary endpoint

- Same measure as Phase 2: pain intensity assessed with a visual analog scale
- Phase 3 will use a responder analysis as proposed by Trevena
  - Defined as ≥30% improvement in sum of pain intensity difference from baseline (SPID) *without* early discontinuation and *without* rescue pain medication
  - Rationale:
    - More straightforward clinical interpretation than pain intensity difference
    - Incorporates an element of safety/tolerability
    - High power based on post-hoc analysis of Phase 2b abdominoplasty data

Post-hoc analysis of phase 2b abdominoplasty data using Phase 3 primary endpoint

	Placebo (n = 39) volume matched	Oliceridine (n = 39) 1.5 mg load, 0.1 mg demand	Oliceridine (n = 39) 1.5 mg load, 0.35 mg demand	Morphine (n = 83) 4.0 mg load, 1.0 mg demand
Responders, n (%)	12 (30.8%)	25 (64.1%)	28 (71.8%)	55 (66.3%)
p-value vs. placebo		0.0005	0.0004	0.0003

Trevena 12



45. Defendants Gowen and Soergel conducted a conference call (where the above slides were presented) on the same day. During the call, Defendant Gowen stated "We welcome the opportunity to work with the FDA to finalize our Phase III plans. I am pleased to report that we had a very productive and collaborative and successful discussion of our oliceridine program with the FDA. This was not only helpful as we transition the program into Phase III, but I'm sure will be invaluable as we continue our conversation throughout the NDA."

46. Trevena repeated many of these same comments in a press release it issued on May 5, 2016 entitled *Trevena Reports First Quarter 2016 Financial Results and Provides Corporate Update*. The release stated in pertinent part:

> Trevena Reports First Quarter 2016 Financial Results
> and Provides Corporate Update
>
> - Results of BLAST-AHF study of TRV027 in acute heart failure expected this month -

- Oliceridine pivotal Phase 3 efficacy studies expected to begin this quarter -

KING OF PRUSSIA, Pa., May 5, 2016 - Trevena, Inc. (NASDAQ: TRVN), a clinical stage pharmaceutical company focused on the discovery and development of biased ligands targeting G protein coupled receptors (GPCRs), today announced financial results for the quarter ended March 31, 2016 and provided an update regarding its ongoing clinical programs.

"The first quarter set the stage for a critical year in Trevena's evolution," said Maxine Gowen, Ph.D., chief executive officer. "**We had a successful End-of-Phase 2 discussion of oliceridine with the FDA**, and look forward to completing our ongoing Phase 3 program aimed at both approval and differentiation of oliceridine for moderate to severe acute pain. In addition, we completed enrollment of the BLAST-AHF Phase 2b Study of TRV027 for acute heart failure and expect to present topline data later this month."

First Quarter and Recent Highlights

· Received Breakthrough Therapy Designation for oliceridine. In February, the U.S. Food and Drug Administration (FDA) granted Breakthrough Therapy designation to the company's lead product candidate, intravenous oliceridine (TRV130), for the management of moderate-to-severe acute pain. Breakthrough Therapy designation is granted by the FDA to new therapies intended to treat serious conditions, and for which preliminary clinical evidence indicates that the drug may demonstrate substantial clinical improvement over available therapies. The company believes this is the first Breakthrough Therapy designation for a pain therapy.

· **Conducted a successful End-of-Phase 2 meeting for oliceridine with the FDA and announced details of the Phase 3 clinical program. Earlier this week, the company announced that it had reached agreement with the FDA on key elements of the Phase 3 program to support a New Drug Application (NDA) for oliceridine. The company also provided additional details of the Phase 3 clinical program, which will include two 375-patient, randomized, double-blind, placebo- and active-controlled, pivotal efficacy trials: the APOLLO-1 study, which will evaluate pain for 48 hours following bunionectomy; and the APOLLO-2 study, which will evaluate pain for 24 hours following abdominoplasty. In each trial, patients will be randomized to receive placebo, morphine, or one of three regimens of**

> **oliceridine by patient-controlled analgesia (PCA) for the management of their post-operative pain, with approximately 75 patients enrolled per study arm. The primary endpoint for both APOLLO studies will be a responder analysis comparing active treatment arms to placebo. Secondary endpoints in both APOLLO studies will include comparisons of oliceridine efficacy, safety, and tolerability to morphine.**
>
> **In January, the company initiated the Phase 3 clinical program with the enrollment of patients in the open label ATHENA study, which is evaluating the safety and tolerability of oliceridine in patients with moderate-to-severe acute pain caused by medical conditions or surgery. Patients will be treated with oliceridine on an as-needed basis via IV bolus, PCA administration, or both, as determined by the investigator.**
>
> The company expects to start the APOLLO studies in the second quarter of this year, and to report top-line data from these studies in the first quarter of 2017. The company continues to expect to file an NDA in the second half of 2017.
>
> · Completed enrollment of the BLAST-AHF study. In April, the company announced that results from its BLAST-AHF Phase 2b study of TRV027 in acute heart failure (AHF) will be presented at Heart Failure 2016, the annual congress of the Heart Failure Association of the European Society of Cardiology, in Florence, Italy. Results of the trial will be presented in a late-breaking trials session scheduled for 2:15-3:45pm CEST on Saturday May 21. The company expects to host a webcast to review the study results following the presentation.

47. Many of the statements made on May 2, 2016 and repeated on May 5, 2016 as described above, were materially false and misleading and omitted to disclose material facts necessary to make the statement made not materially false or misleading. The table below summarizes these statements, and explains why each statement was materially false or misleading when made and the omitted material facts:

Statement	**Why the Statement Was Materially False or Misleading**
Trevena: "The company has reached general agreement with the FDA on key elements of the Phase 3 program to support a New Drug Application (NDA) for oliceridine (TRV130)." ¶ 43.	Trevena's investor presentation lists "key elements" of the Phase 3 program, among which are: two pivotal efficacy studies with PCA dosing to support potential finding of efficacy; and safety database with PCA and bolus dosing ≥ 1,100 patients, including a sufficient number of patients with higher exposures and longer durations of oliceridine therapy. ¶ 44. Trevena failed to disclose that the FDA: instructed Trevena to modify all protocols for ongoing clinical trials to include certain safety assessments; did not agree with the proposed dosing in the Phase 3 studies; did not agree with the proposed primary endpoint; did not agree with the proposed non-inferiority margin for comparing morphine to oliceridine; required a safety database of at least 350 patients exposed to the highest intended dose for the longest expected duration of use; required any comparative safety claims to be replicated, adequately justified for clinical relevance, and established in the setting of comparable efficacy between comparators to be considered for inclusion in labeling. ¶¶ 33, 41. The foregoing disagreements and issues raised by the FDA relate directly to the pivotal efficacy studies and the primary and secondary endpoints thereto, as well as the safety study. The omission of these critical disagreements regarding the key elements of the Phase 3 program rendered Trevena's statements materially false and misleading.
Trevena: "Trevena Announces Successful End-of-Phase 2 Meeting with FDA. . ." ¶ 43. Trevena: "Trevena . . . today announced the successful completion of the End-of-Phase 2 Meeting process with the United States Food and Drug Administration (FDA)." ¶ 43.	In light of Defendants' statement that "The Company had reached general agreement with the FDA on key elements of the Phase 3 program" a reasonable person, reading Defendants' statements concerning the success of the End-of-Phase 2 meeting and being "very pleased" with the outcome of the meeting, would understand that Trevena's

Gowen: "We are very pleased with the outcome of our End-of-Phase 2 discussion with the FDA. . .". ¶ 43. Gowen: "[W]e had a very productive and collaborative and successful discussion of our oliceridine program with the FDA." ¶ 45.	executives believed that the FDA did in fact agree with the key elements of the Phase 3 program, and all that stood in the way of gaining approval was successfully implementing the program as it had been presented to the FDA. Despite being aware of the FDA's disagreements regarding the key elements of the Phase 3 program, Trevena and Defendant Gowen made statements concerning the success of the End-of-Phase 2 Meeting" and being "very pleased" with the End-of-Phase 2 discussions with the FDA. The omitted facts, known to Defendants, were necessary to make the statements concerning the success of the End-of-Phase 2 meeting with the FDA not materially misleading.
Trevena: "[Safety] database should include a sufficient number of patients with higher exposures and longer durations of oliceridine therapy." ¶ 43.	Trevena omitted to disclose that the FDA informed them "that the safety database **must include at least 350 patients exposed to the highest intended dose for the longest expected duration of use.**" ¶ 41. Trevena's materially incomplete description of the FDA's safety database requirements are particularly misleading given that the FDA did not agree with Trevena's proposed dosing as the Company had not previously studied doses even half of the levels proposed for Phase 3 and did not have adequate non-clinical support for the proposed dosing. ¶ 41. Investors were thus unaware that the FDA had set forth strict minimum requirements for the safety database, why those requirements were set, and that satisfying those requirements was critical to Trevena's chances for approval.
Trevena: "The primary endpoint for both [Phase 3 pivotal efficacy] studies will be a responder analysis proposed by the company comparing active treatment arms to placebo. A responder is defined as a patient experiencing a sum of pain intensity difference (SPID) at the end of the treatment period that corresponds to at least a 30% improvement from baseline without early	Trevena omitted to disclose that the FDA "did not agree with the proposed primary endpoint, as it was unclear how a 30% improvement from baseline based on SPID correlates to an improvement in pain intensity scores on the NRS in the proposed setting of acute postoperative pain and if that change is clinically relevant." ¶ 41.

discontinuation and without rescue pain medication." ¶ 43.	Trevena listed the pivotal efficacy trials to which the primary endpoint applied as a "key element" of the Phase 3 program in its investor presentation (¶ 44), rendering the statement that it reached general agreement with the FDA on "key elements of the Phase 3 program" materially false and misleading.
Trevena: "Secondary endpoints in both [Phase 3 pivotal efficacy] studies will include comparisons of oliceridine efficacy, safety, and tolerability to morphine. A respiratory safety endpoint will measure prevalence and duration of hypoventilation, which will be a clinical assessment as in the company's Phase 2b abdominoplasty study." ¶ 43.	Trevena failed to disclose that the FDA "did not agree with the proposed non-inferiority (NI) margin for comparing morphine to oliceridine" and that "[a]ny comparative safety claims must be replicated, adequately justified for clinical relevance, and established in the setting of comparable efficacy between comparators to be considered for inclusion in labeling." ¶ 41. These secondary endpoints applied to the pivotal efficacy trials listed as a "key element" of the Phase 3 program (¶ 44) on which Trevena claimed to have reached agreement with the FDA. Omitting to disclose these disagreements concerning key elements of the Phase 3 trials and issues raised by the FDA rendered Trevena's description of the secondary endpoints materially false and misleading.
Trevena: "[Phase 3 pivotal efficacy] study designs were informed in part by the company's Phase 2b abdominoplasty study, which also used PCA dosing. Powering assumptions included similar performance of PCA-administered oliceridine in both APOLLO studies as was observed in the Phase 2b study. In a post-hoc evaluation using the Phase 3 responder analysis, both doses in the company's Phase 2b study in abdominoplasty yielded analgesic efficacy similar to morphine, and significantly higher than placebo ($p < 0.0005$ for both oliceridine treatment arms). In addition, using the Phase 3 respiratory safety endpoint, both doses in the company's Phase 2b study showed significantly less respiratory safety burden for	Trevena omitted to disclose that the FDA "did not agree with the proposed dosing in the Phase 3 studies. The Sponsor proposed dosing up to 100 mg daily (including a 0.75 mg every 1 hour as needed clinician administered dose), but had only studied maximum daily doses of 36.8 mg. Further, the Sponsor did not have adequate non- clinical support for the proposed doses." ¶ 41. Trevena also omitted to disclose that the FDA "did not agree with the proposed non-inferiority (NI) margin for comparing morphine to oliceridine[.]" ¶ 41. Omitting to disclose these disagreements concerning key elements of the Phase 3 trials rendered Trevena's description of the Phase 3 study designs materially false and misleading, particularly in light of the Company's claim

oliceridine than morphine ($p < 0.0003$ for both oliceridine treatment arms).” ¶ 43.	that it had reached general agreement with the FDA on “key elements” of the Phase 3 program.
Trevena: “The development program will include at least 1,100 patients exposed to oliceridine. The on-going open-label ATHENA-1 safety study is enrolling patients experiencing pain as a result of either a medical diagnosis or surgery. In this study, patients may receive oliceridine as-needed either as an intermittent bolus or via PCA device, with doses and durations appropriate to manage their pain.” ¶ 43.	Trevena omitted to disclose that the FDA did not agree with the proposed dosing in the Phase 3 studies and that as a result, the FDA set minimum criteria for the safety database – requiring at least 350 patients exposed to the highest intended dose for the longest expected duration of use. ¶ 41. Furthermore, the Company omitted to disclose that the ATHENA-1 study was designed in a manner that would prevent it from meeting the FDA’s requirement of a safety database that includes at least 350 patients exposed to the highest intended dose for the longest expected duration of use. As a result of these omissions of material facts, Trevena’s description of the safety study was materially false and misleading, particularly in light of the Company’s claim that it had reached general agreement with the FDA on “key elements” of the Phase 3 program.

48. During the May 2, 2016 conference call, Defendant Gowen told investors “**Our confidence in the plans we presented to the agency** going into the end of Phase 2 meeting, **led us to initiate much of the preparatory work for our pivotal efficacy studies *ahead of the meeting***; and I’m happy to share that, that decision has paid off and we will be commencing both of our pivotal efficacy studies this quarter.” Later in the call, Gowen reiterated, “**we did quite a lot of the study start up at risk** because we were fairly confident in our pivotal study design that we submitted to the FDA. **We’re very happy now that we did that because it really allows us to start very quickly now**.”

49. Defendants took a calculated gamble and lost it. They bet the FDA would agree with their proposals for the Phase 3 studies and, as Gowen admitted, they did a lot of work “ahead

of the meeting" "at risk." Rather than admit their failure and waste of time, money and effort, Defendants simply moved forward with the work they already started in spite of the FDA's disagreements with them. While Trevena was representing to investors about their supposedly "successful" meeting with the FDA, they were also lobbying the agency about Trevena's proposed endpoint and responder definition, which Trevena knew the FDA did not agree with. Trevena's hubris led them to set up the Phase 3 program at risk so that they would be able to move forward immediately after the end of Phase 2 meeting. When the FDA disagreed with the key elements of Trevena's Phase 3 program, the Company attempted to push its plan through rather than take the time and resources to redesign the Phase 3 program to the FDA's satisfaction.

50. A reasonable person, reading Defendant Gowen's statements concerning the benefits of having frontloaded the Phase 3 program design prior to the End-of-Phase 2 meeting, would understand that Trevena's executives believed that the FDA agreed with the key elements of their Phase 3 program, and all that stood in the way of securing approval for oliceridine was successfully implementing the program as it had been presented to the FDA. Gowen omitted the known material facts, that the FDA disagreed with the key elements of the Phase 3 program, which were necessary to make her statement regarding the benefits of having initiated the Phase 3 program design ahead of the End-of-Phase 2 meeting not misleading. Rather than "allow[ing] [Trevena] to start very quickly now," the real facts were that Trevena had already started—at risk—a Phase 3 program which the FDA disagreed with, and Trevena would not be able or willing to modify the program as a result of the FDA's disagreements.

51. Indeed, just days after touting the success and agreement with the FDA, on May 6, 2016, unbeknownst to investors, Trevena submitted to the FDA a justification for their proposed responder definition, which the FDA had previously rejected.

52. Omitting to disclose the FDA's disagreement with Trevena's proposed primary endpoint while concealing Trevena's ongoing attempt to justify its rejected primary endpoint rendered the statements concerning the benefits of preparing the Phase 3 study at risk, set forth in paragraphs 48 and 49, materially false and misleading.

53. Defendants Gowen and Soergel apparently attended the March 29, 2016 meeting with the FDA and received and reviewed the FDA's minutes from that meeting. Soergel stated on May 2 "***we*** held our end of Phase 2 meeting at the end of March and ***we*** recently received the final meeting minutes from the FDA." Similarly, Gowen stated "***we've*** had a very successful end of Phase 2 meeting with the FDA. **We heard** that it is appropriate to move oliceridine into Phase 3 . . ."

54. Even if neither Gowen nor Soergel attended the March 29, 2016 End-of-Phase 2 meeting in person, they were reckless in discussing what occurred at the meeting, what the FDA purportedly agreed with without first reviewing the minutes of the meeting that were sent to Trevena. As a start-up bio-tech company dependent on a single drug's obtaining approval from the FDA, its senior officers either knew of what actually happened at the End-of-Phase 2 meeting and read the meeting minutes or discussed what transpired at the meeting in reckless disregard for the truth.

55. On May 16, 2016, Trevena announced that its only other major drug candidate, TRV027, "failed to meet either the primary or secondary endpoints" during its Phase 2 trial. Trevena made clear to investors that, as a result, it "expects to focus its efforts on its lead Phase 3 oliceridine pain program and its earlier stage programs," and that there were no other drugs far along in the development pipeline for Trevena besides oliceridine.

56. On June 8, 2016, Trevena issued a press release entitled *Trevena, Inc. Announces First Patients Enrolled in the APOLLO-1 and APOLLO-2 Phase 3 Pivotal Efficacy Studies of Oliceridine in Acute Pain*. In part, the press release stated:

> Trevena, Inc. (NASDAQ: TRVN), a clinical stage biopharmaceutical company focused on the discovery and development of biased ligands targeting G protein coupled receptors, today announced the enrollment of the first patients in the Phase 3 APOLLO-1 and APOLLO-2 studies of oliceridine in patients suffering moderate to severe acute pain following bunionectomy and abdominoplasty, respectively.
>
> "We are pleased to announce the start of the APOLLO studies, which we designed both to support approval of oliceridine and to confirm the potential differentiation of oliceridine from conventional opioids," commented Maxine Gowen, Ph.D., chief executive officer. **"The trials recapitulate many features of our successful Phase 2 studies, with refinements based on the full Phase 2 data set that we believe strengthen the study designs and improve our probability of success. Together with the ongoing ATHENA Phase 3 safety study, we believe the APOLLO studies position us to deliver a robust data package to support regulatory approval and commercial success."**
>
> The company continues to expect to report top-line data from both APOLLO studies in the first quarter of 2017, and to file an NDA for oliceridine in the second half of 2017. The company also continues to expect that its available cash and investments will be sufficient to fund operations into 2018.
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> About the APOLLO-1 and APOLLO-2 Studies
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> Both APOLLO trials are phase 3, multicenter, randomized, double-blind, placebo- and active-controlled studies of oliceridine for the treatment of moderate to severe acute pain. The APOLLO-1 study will evaluate pain for 48 hours following bunionectomy, and the APOLLO-2 study will evaluate pain for 24 hours following abdominoplasty. In each trial, patients will be randomized to receive placebo, morphine, or one of three regimens of oliceridine by patient-controlled analgesia (PCA) device for the management of their post-operative pain. Each study will enroll approximately 375 patients, allocated equally across study arms. **The primary objective in each study is to evaluate the analgesic efficacy of oliceridine compared to placebo. Secondary endpoints will**

include comparisons of oliceridine efficacy, safety, and tolerability to morphine.

57. Defendant Gowen's statement that "we believe the APOLLO studies position us to deliver a robust data package to support regulatory approval and commercial success," contained a material omission, in that the statement fails to explain that the FDA had: instructed Trevena to modify all protocols for ongoing clinical trials; disagreed with the proposed dosing due to a lack of prior clinical data and non-clinical support for the proposed doses; and disagreed with the proposed non-inferiority margin for comparing morphine to oliceridine, as described in ¶¶ 33, 41, 47, above.

58. Trevena's description of the primary and secondary endpoints of the study contains a material omission, in that the statement fails to explain that the FDA disagreed with the use of the primary endpoint proposed by Trevena, the proposed dosing regimen, as well as the methods by which Trevena intended to prove its proposed secondary endpoints as described in ¶¶ 41, 47, above.

59. Also, on June 8, Gowen presented on behalf of Trevena at the Jefferies Healthcare Conference. During her opening remarks, Gowen stated "So, we had an end of Phase 2 meeting with the FDA at the very end of March. And we reached agreement with them that we have shown sufficient data to move into Phase 3. The program that we proposed to them they agreed would support an approval – could support, I should say given that the data are correct, could support an approval for the target indication." Gowen further stated "The key elements of the Phase 3 program are two pivotal efficacy studies with PCA dosing as I – in the study I just showed you in Phase 2, to support efficacy. . . . And this is what allows us to get this broad label."

60. Gowen's statement regarding the FDA's comments at the end of Phase 2 meeting at the end of March 2016 were materially false and misleading. The statement that the FDA

"agreed" that the "program [Trevena] proposed to them . . . could support an approval for the target indication" is directly contradicted by the FDA's minutes from that Phase 2 meeting, as described in ¶¶ 41, 47, where the FDA informed Trevena that it did not agree with the proposed dosing or primary endpoint for the pivotal efficacy studies, which Gowen herself described as "key elements of the Phase 3 program."

61. Furthermore, Gowen's description of the Phase 3 efficacy studies contained material omissions in that the statements described the studies as being able to get Trevena a "broad label" from the FDA without disclosing that the FDA, during its March 2016 meeting with Trevena, stated that "[a]ny comparative safety claims must be replicated, adequately justified for clinical relevance, and established in the setting of comparable efficacy between comparators to be considered for inclusion in labeling," as described in ¶¶ 41, 47. At the same March 2016 meeting, the FDA also stated that it "did not agree with the proposed non-inferiority (NI) margin for comparing morphine to oliceridine." ¶¶ 41, 47. Since the FDA disagreed with Trevena's proposed method for comparing morphine to oliceridine, and informed the Company that comparative safety claims had to be established in the setting of comparable efficacy between comparators [i.e. morphine] to be considered for inclusion on the label, Trevena's chances of obtaining a "broad label" from the FDA were far from likely. This is directly contrary to what Trevena presented to investors.

62. On June 21, 2016, Defendant Soergel presented at the JMP Securities Life Sciences Conference. During his opening remarks, Soergel stated "The Phase III timing and expectations, as you can see here, we've initiated our Phase III program. The ATHENA study was initiated in the first quarter. The two pivotal efficacy trials were initiated in the second quarter. We expect the

data from our Phase III pivotal efficacy studies in the first quarter of 2017 with an NDA submission in the second half of 2017. And hopefully, we can get this important new drug to patients quickly."

63. This statement contained a material omission in that Soergel stated that Trevena expected to submit its New Drug Application in the second half of 2017 without disclosing that the FDA had: previously informed Trevena of the need to modify all protocols for ongoing clinical trials; did not agree with the proposed dosing; did not agree with the proposed primary endpoint; did not agree with the proposed non-inferiority margin for comparing morphine to oliceridine; warned that comparative safety claims would have to satisfy stringent requirements to be considered for inclusion in labeling; and had set forth strict criteria for the safety database due to concerns about Trevena's proposed dosing, as described in ¶¶ 33, 41, 47, greatly decreasing the likelihood of success of that NDA.

64. On August 3, 2016, Trevena issued a press release announcing its second quarter 2016 financial results. The press release stated in part:

> "This quarter marked an important milestone for the company's oliceridine program with the initiation of our two Phase 3 pivotal efficacy trials," said Maxine Gowen, Ph.D., chief executive officer. **"Following our successful End-of-Phase-2 and Breakthrough Therapy designation meeting with the FDA in the first quarter, we were able to rapidly initiate the pivotal efficacy trials, which are enrolling well."**
>
> Second Quarter and Recent Highlights
>
> Enrolled first patients in APOLLO-1 and APOLLO-2 Phase 3 trials of oliceridine. In June, the company announced the enrollment of the first patients in the APOLLO-1 and APOLLO-2 pivotal Phase 3 efficacy studies. APOLLO-1 is studying patients suffering moderate to severe pain for 48 hours after undergoing bunionectomy, while APOLLO-2 is studying patients suffering moderate to severe pain for 24 hours after undergoing abdominoplasty; both are 375-patient, multicenter, randomized, double-blind, placebo- and active-controlled studies. Patients are randomized to receive placebo, morphine, or one of three oliceridine regimens, all dosed as needed

> via patient-controlled analgesia (PCA) device for the management of their post-operative pain, with approximately 75 patients per study arm. **The primary objective of both trials is to evaluate the analgesic efficacy of oliceridine versus placebo. Secondary endpoints compare the efficacy, safety, and tolerability of oliceridine to morphine. The company continues to expect to release top-line data in the first quarter of 2017 and to file an NDA in the second half of 2017.**

65. The statement made by Gowen regarding Trevena's "successful End-of-Phase 2 and Breakthrough Therapy designation meeting with the FDA in the first quarter," was materially false in that the End-of-Phase 2 meeting was not successful, given that the meeting resulted in the FDA informing Trevena that it did not agree with the proposed dosing, the proposed primary endpoint, or the proposed non-inferiority margin for comparing morphine to oliceridine, as described in ¶¶ 41, 47, above. The FDA had also warned that comparative safety claims would have to satisfy stringent requirements to be considered for inclusion in labeling, and had set forth strict criteria for the safety database due to concerns about Trevena's proposed dosing, as described in ¶¶ 41, 47, above.

66. The description Trevena provided of the endpoints of their Phase 3 studies contained material omissions in that the statement failed to disclose that the FDA had disagreed with Trevena's use of the endpoint proposed by Trevena, as described in ¶¶ 41, 47.

67. Trevena's statement that it "continues to expect to . . . file an NDA in the second half of 2017" omitted to disclose material facts as the statement failed to disclose that the FDA had: previously informed Trevena of the need to modify all protocols for ongoing clinical trials; did not agree with the proposed dosing; did not agree with the proposed primary endpoint; did not agree with the proposed non-inferiority margin for comparing morphine to oliceridine; warned that comparative safety claims would have to satisfy stringent requirements to be considered for inclusion in labeling; and had set forth strict criteria for the safety database due to concerns about

Trevena's proposed dosing, as described in ¶¶ 33, 41, 47 above, and was thus unlikely to approve Trevena's New Drug Application.

68. On November 3, 2016, Trevena issued a press release announcing its third quarter 2016 financial results. The press release stated in part:

> This quarter saw important progress for our company, with continued execution of our Phase 3 program for oliceridine. We had extensive engagement with the medical community to discuss the challenges of acute pain management in the hospital and how oliceridine may provide an important treatment option to patients and physicians," said Maxine Gowen, Ph.D., chief executive officer. "We look forward to sharing top-line data from both Phase 3 APOLLO pivotal efficacy studies in the first quarter of 2017, and filing an NDA in the second half of next year."
>
> Third Quarter and Recent Highlights
>
> APOLLO-1 and APOLLO-2 Phase 3 efficacy trials of oliceridine remain on track for first quarter 2017 top-line data release. The APOLLO-1 trial includes patients suffering moderate to severe pain after undergoing bunionectomy, while the APOLLO-2 trial includes patients suffering moderate to severe pain after undergoing abdominoplasty; both are 375-patient, multicenter, randomized, double-blind, placebo- and active-controlled studies. **Patients are randomized to receive placebo, morphine, or one of three oliceridine regimens, all dosed as needed via patient-controlled analgesia (PCA) device** for the management of their post-operative pain, with approximately 75 patients per study arm. **The primary objective of both trials is to evaluate the analgesic efficacy of oliceridine versus placebo. Secondary endpoints compare the efficacy, safety, and tolerability of oliceridine to morphine.**
>
> **Patient enrollment remains on track in the ATHENA multi-procedure safety study of oliceridine to support NDA filing in 2H 2017.** This trial complements the APOLLO studies and aims to evaluate the safety and tolerability of oliceridine in patients with moderate to severe acute pain caused by a broad range of medical conditions or surgeries. Patients are treated on an as-needed basis via IV bolus, PCA administration, or both, as determined by the investigator.

69. The description Trevena provided of the dosing for the Phase 3 studies contained material omissions in that the statement failed to disclose that the FDA had disagreed with Trevena's proposed dosing in the Phase 3 studies, as described in ¶¶ 41, 47.

70. Likewise, the description Trevena provided of the primary and secondary endpoints of the Phase 3 studies contained material omissions in that the statement failed to disclose that the FDA had disagreed with Trevena's use of the primary and secondary endpoints proposed by Trevena, as described in ¶¶ 41, 47.

71. Trevena's statement that "[p]atient enrollment remains on track in the ATHENA multi-procedure safety study of oliceridine to support NDA filing in 2H 2017" and subsequent description of the safety study contained material omissions in that the statement failed to disclose that the FDA had instructed Trevena to "modify all protocols for ongoing clinical trials" to include certain safety assessments, as described in ¶ 33. The statement also failed to disclose that the FDA had provided explicit minimum criteria for the safety database due to concerns about Trevena's proposed dosing regimen, as described in ¶¶ 41, 47. As discussed in ¶¶ 118-19, below, Trevena failed to implement the safety assessments as instructed by the FDA and failed to ensure that the safety database satisfied the FDA's minimum criteria, and was thus unlikely to gain approval for the NDA.

72. On November 8, 2016, unbeknownst to investors and the marketplace, Trevena held a teleconference with the FDA concerning the agency's disagreement with Trevena's proposed method for evaluating the respiratory safety of oliceridine as compared to morphine. The agency sent written minutes to Trevena from this meeting on December 19, 2016. These written minutes, which were shared only with Trevena, stated directly:

> FDA did not agree with Trevena's proposal to evaluate the respiratory safety of oliceridine as compared to morphine because

> the definition of Respiratory Safety Events (RSEs) was not clearly defined and the determination of the presence of an RSE relied largely on clinical acumen. Even though the parameters proposed in the evaluation of an RSE (respiratory rate, oxygen saturation, and MRPSS somnolence/sedation scores) are well accepted criteria used for the assessment of patients at risk for experiencing an RSE, it is unclear that a small change in these parameters is of clinical significance. Trevena was told to specify a clinically meaningful definition of an RSE, such as patients who require a clinical intervention after meeting a specific criterion (e.g., naloxone administration and/or oxygen administration with a reduction in oxygen saturation). Further, FDA did not agree with inclusion of sedation and somnolence in the RSE definition.
>
> FDA stated that the statistical model proposed to evaluate the respiratory safety of oliceridine incorporates both the population prevalence of RSEs and the population conditional mean cumulative duration of RSEs to describe respiratory safety burden (RSB). Based on this model, a small change in event duration could result in a statistically significant result without clinical significance. In addition, the RSB endpoint is difficult to interpret and apply directly to clinical practice. Trevena was asked to analyze and report event duration separately from the event prevalence.

73. On January 4, 2017, Trevena issued a press release entitled *Trevena Completes Enrollment of Phase 3 APOLLO Pivotal Efficacy Trials of Oliceridine for Moderate-to-Severe Acute Pain*. In part, the press release stated:

> Trevena, Inc. (NASDAQ:TRVN) today announced that it has completed enrollment of its Phase 3 APOLLO-1 and APOLLO-2 pivotal efficacy studies of oliceridine (TRV130) in moderate-to-severe acute pain following bunionectomy and abdominoplasty, respectively.
>
> "We are pleased to have completed enrollment in these important studies and to confirm that the APOLLO trials remain on schedule to report top-line results in the first quarter of 2017," said Maxine Gowen, Ph.D., chief executive officer. "We look forward to sharing these data when they become available."
>
> **The APOLLO studies were designed based on the Phase 2 clinical trials of oliceridine that were successful in showing potential differentiation of oliceridine from morphine. The Company expects top-line results to include measures of**

> **efficacy, safety, and tolerability of oliceridine compared to both placebo and morphine.**
>
> **In addition, the Company announced that patient enrollment for the Phase 3 ATHENA multi-procedure safety study remains on track. The Company continues to anticipate filing a New Drug Application (NDA) for oliceridine with the U.S. Food & Drug Administration (FDA) in the second half of 2017.**
>
> **About the APOLLO-1 and APOLLO-2 Studies**
>
> Both APOLLO trials are Phase 3, multicenter, randomized, double-blind, placebo- and active-controlled studies of oliceridine for the treatment of moderate to severe acute pain. The APOLLO-1 study is evaluating pain for 48 hours following bunionectomy, and the APOLLO-2 study is evaluating pain for 24 hours following abdominoplasty. **In each trial, patients were randomized to receive placebo, morphine, or one of three regimens of oliceridine by patient-controlled analgesia (PCA) device for the management of their post-operative pain.** Each study enrolled approximately 375 patients, allocated equally across study arms. **The primary objective in each study is to evaluate the analgesic efficacy of oliceridine compared to placebo. Secondary endpoints include comparisons of efficacy, safety, and tolerability of oliceridine to morphine.**

74. The description Trevena provided concerning the design of the Phase 3 studies contained material omissions in that the statement failed to disclose that the FDA had disagreed with Trevena's proposed dosing, the primary endpoint, and the methods by which Trevena planned to prove its secondary endpoints, as described in ¶¶ 41, 47, above.

75. The statement that Trevena expected the study results to include "measures of … safety . . . of oliceridine compared to both placebo and morphine" was also materially false and misleading in that it failed to disclose that in November of 2016, the FDA informed Trevena that it "did not agree with Trevena's proposal to evaluate the respiratory safety of oliceridine as compared to morphine" as described in ¶ 72, above.

76. Furthermore, Trevena's statement that the "ATHENA multi-procedure safety study remains on track" contained material omissions in that the statement failed to disclose that the

FDA had explicitly instructed Trevena that the safety database must include at least 350 patients exposed to the highest intended dose for the longest expected duration of use, as described in ¶¶ 41, 47, above. Trevena also failed to disclose that this requirement was due to the FDA's disagreement with Trevena's proposed dosing of 100 mg daily, given that Trevena had only studied maximum daily doses of 36.8 mg and did not have adequate non-clinical support for the proposed dosing, as described in ¶¶ 41, 47, above. Indeed, an FDA Briefing Document would later reveal that during the review cycle, Trevena "modified the recommended maximum daily dose and dosing instructions . . . several times" including reducing the maximum daily dose "from 100 mg daily to 40 mg daily to try to address the adequacy of the safety database[.]" Even with the undisclosed modifications, the FDA Briefing Document shows that Trevena was never able satisfy the safety database requirements – instead the highest daily dose that had at least 350 patients exposed was only 27 mg, and the highest dose with the longest actual duration that had at least 350 patients was only 37.2 mg over a period of 35.5 hours, as described in ¶ 119, below. Not only was Trevena never "on track" to complete the safety study to the FDA's satisfaction, it was also covertly reducing the maximum daily dose and dosing instructions in the hopes of producing acceptable results.

77. On February 21, 2017, Trevena issued a press release entitled *Trevena Announces Positive Top-line Results from Two Phase 3 Pivotal Efficacy Studies on Intravenous Oliceridine in Moderate-to-Severe Acute Pain*. In part, the press release stated:

> Trevena, Inc. (NASDAQ: TRVN) today announced positive top-line results from its Phase 3 APOLLO-1 and APOLLO-2 pivotal efficacy studies of oliceridine in moderate-to-severe acute pain following bunionectomy and abdominoplasty, respectively. In both studies, all dose regimens achieved their primary endpoint of statistically greater analgesic efficacy than placebo, as measured by responder rate. In addition, oliceridine showed dose-related trends of improvements vs. morphine on numerous measures of respiratory

safety and gastrointestinal tolerability — both key unmet needs in acute pain management.

"These data are exciting — they confirm earlier data, and show an improved safety and tolerability profile of oliceridine compared to morphine, with very similar results across the two studies," said Timothy Beard, M.D., FACS, Chair of Department of Surgery, Bend Memorial Clinic, Oregon.

"We believe the data for all three dose regimens will support FDA approval of IV oliceridine with a broad indication of management of moderate-to-severe acute pain. These successful trials cap a development program that has shown consistent differentiation of oliceridine from morphine in multiple clinical trials," said Maxine Gowen, Ph.D., chief executive officer. "We look forward to submitting a new drug application with the goal of bringing this innovative product to patients."

Both APOLLO trials were Phase 3, multicenter, randomized, double-blind, placebo- and active-controlled studies of oliceridine. The primary objective of each study was to evaluate the analgesic efficacy of oliceridine compared to placebo. Secondary endpoints included comparisons of efficacy, safety, and tolerability of oliceridine to morphine. Both studies included multiple measurements of nausea and vomiting, which occur in approximately 30% of postoperative patients and increase costs to hospitals, as well as multiple measures of respiratory safety, which can pose serious and costly risks to patient safety.

* * *

Oliceridine program update

The Company also announced that patient enrollment for the Phase 3 ATHENA multi-procedure safety study remains on track, with over 400 patients treated with oliceridine and no apparent off-target or unexpected adverse effects to date. In addition, a recently completed renal impairment study suggests that no dose adjustment will be required in renally impaired patients, and a metabolism study showed no evidence of active metabolites. These data distinguish oliceridine from conventional opioids – particularly in at-risk patients for whom safe opioid titration can be challenging. All additional clinical, non-clinical, and manufacturing activities remain on track to support an NDA submission in the fourth quarter of this year.

78. The results Trevena reported concerning the Phase 3 efficacy trials, that "[i]n both studies, all dose regimens achieved their primary endpoint of statistically greater analgesic efficacy than placebo, as measured by the responder rate" contained material omissions in that the statement failed to disclose that the FDA had disagreed with Trevena's proposed dosing and primary endpoint, as described in ¶¶ 41, 47, above.

79. Trevena's statement that "oliceridine showed dose-related trends of improvements vs. morphine on numerous measures of respiratory safety and gastrointestinal tolerability" also contained material omissions in that the statement failed to disclose that the FDA had disagreed with Trevena's proposed non-inferiority margin for comparing morphine to oliceridine and did not agree with Trevena's proposal to evaluate the respiratory safety of oliceridine as compared to morphine, as described in ¶¶ 41, 47, 72, above.

80. Furthermore, Defendant Gowen's statement that "We believe the data for all three dose regimens will support FDA approval of IV oliceridine with a broad indication" and that the "successful trials . . . ha[ve] shown consistent differentiation of oliceridine from morphine in multiple clinical trials" contained material omissions because the statement failed to disclose that the FDA had disagreed with Trevena's proposed dosing, primary endpoint, an non-inferiority margin for comparing morphine to oliceridine, as described in ¶¶ 41, 47, above.

81. The description of the Phase 3 studies including "multiple measures of respiratory safety" also contained material omissions in that the statement failed to disclose that the FDA did not agree with Trevena's proposal to evaluate the respiratory safety of oliceridine as compared to morphine, as described in ¶ 72, above.

82. Furthermore, Trevena's discussion of the Phase 3 study results contained material omissions in that the statement failed to disclose that the FDA had instructed the Company to

"submit amendments to modify all protocols for ongoing clinical trials" to include certain safety assessments, because Trevena's Phase 2 study saw "QTcF prolongation [which] exceeded the 10-ms regulatory threshold at clinically relevant exposures" as described in ¶ 33, above. Unbeknownst to investors, Trevena failed to implement the additional safety assessments, leading the FDA to conclude that "the limited ECG monitoring data [which the FDA had instructed Trevena to collect] in Phase 3 do not appear adequate to evaluate the QT effects of oliceridine" as described in ¶ 119, below.

83. Also on February 21, 2017, Defendants Gowen and Soergel held a conference call to discuss the top-line results for the Phase 3 efficacy studies. In addition to repeating the false statements described in ¶¶ 77-82 above, Defendant Gowen acknowledged during the call that "[a] particular challenge was including morphine as a comparator in the trial, not the norm in our industry, and we took this step once again in order to demonstrate the benefit of this innovative next-generation opioid compared head to head to conventional opioids. . . . [W]e delivered two highly successful trials." Gowen's statement contained material omissions in that it failed to disclose that the FDA did not agree with Trevena's proposed non-inferiority margin for comparing morphine to oliceridine and that the FDA had informed Trevena that any comparative safety claims would have to be established in the setting of comparable efficacy between comparators to be considered for inclusion in labeling, as described in ¶¶ 41, 47, above.

84. During the call, Defendant Soergel also discussed Trevena's use of a responder analysis to assess the primary efficacy endpoint, explaining that Trevena "use[d] this analysis because it reflects the efficacy in the cleanest way." Soergel's statement contained material omissions in that it failed to disclose that the FDA did not agree with Trevena's use of a responder analysis in its proposed primary endpoint, as described in ¶¶ 41, 47, above.

85. Defendant Soergel also discussed the secondary endpoints, "including respiratory safety compared to morphine and non-inferiority on efficacy compared to morphine." Soergel's discussion contained material omissions in that it failed to disclose that the FDA did not agree with Trevena's proposed non-inferiority margin for comparing morphine to oliceridine and did not agree with Trevena's proposal to evaluate the respiratory safety of oliceridine as compared to morphine, as described in ¶¶ 41, 47, 72, above.

86. On March 8, 2017, Trevena issued a press release announcing its fourth quarter and fiscal year 2016 financial results. The press release stated in part:

> "The recent successful completion of the pivotal efficacy studies for OLINVO puts us in a strong position to bring this innovative analgesic to physicians and patients in need of a new option for managing moderate-to-severe acute pain in the hospital," said Maxine Gowen, Ph.D., chief executive officer. "We believe the data from these studies highlight the potential for OLINVO to reduce the burden of opioid-related adverse effects, particularly for those patients who are at elevated risk for serious consequences from post-operative nausea and vomiting or opioid-induced respiratory depression."
>
> **2016 and recent corporate highlights**
>
> * * *
>
> **Successful End-of-Phase 2 meeting with FDA.** In May 2016, the Company announced that it had reached general agreement with the FDA on key elements of the Phase 3 OLINVO program to support a New Drug Application (NDA), including that the APOLLO-1 and APOLLO-2 pivotal efficacy trials in bunionectomy and abdominoplasty included appropriate patient populations to support and indication for moderate-to-severe acute pain.
>
> **In February 2017, announced positive top-line results from two Phase 3 pivotal efficacy studies of OLINVO in moderate-to-severe acute pain.** OLINVO demonstrated fast onset and strong opioid efficacy in hard tissue and soft tissue pain models, supporting the Company's planned NDA submission and a potential indication for the management of moderate-to-severe acute pain. Numerous measures of respiratory safety and gastrointestinal tolerability all

> showed trends of meaningful improvements for OLINVO compared to a commonly used IV morphine regimen.
>
> **Initiated Phase 3 ATHENA open label safety study of OLINVO.** In January 2016, the Company announced the launch of the OLINVO Phase 3 clinical program with the enrollment of patients in the open label Phase 3 ATHENA study. This study is evaluating the safety and tolerability of OLINVO in patients with acute moderate-to-severe pain in a variety of surgical settings. As of February 15, 2017, more than 400 patients have been treated with OLINVO, with no apparent off-target or unexpected drug-related adverse effects to date. The Company remains on track to submit an NDA for OLINVO in the fourth quarter of 2017.

87. Trevena's description of its "successful" End-of-Phase 2 meeting with the FDA, in which it claimed to have reached general agreement with the FDA on "key elements" of the Phase 3 program contained material omissions in that the statement failed to disclose the FDA's disagreement with the key elements of the Phase 3 program, including Trevena's proposed dosing, primary endpoint, non-inferiority margin for comparing morphine to oliceridine, and how Trevena would prove its secondary endpoints, as described in ¶¶ 41, 47, above.

88. The overview of the "positive" top-line results from the Phase 3 efficacy trials, including that the studies demonstrated "strong opioid efficacy" to support the Company's planned NDA, as well as the claims of meaningful improvement in respiratory safety compared to morphine also contained material omissions in that the statements failed to disclose that the FDA did not agree with Trevena's proposed primary endpoint and did not agree with Trevena's proposal to evaluate oliceridine's respiratory safety as compared to morphine, as described in ¶¶ 41, 47, 72, above.

89. Furthermore, the statement that the ATHENA safety study "remains on track" contained a material omission in that it failed to disclose that the FDA had set minimum criteria for the safety database due to concerns about Trevena's proposed dosing regimen, as described in ¶¶ 41, 47, above. The statement also failed to disclose that Trevena was never "on track" to

complete the study to the FDA's satisfaction, despite having modified the proposed maximum dosing and dosing instructions on multiple occasions in order to address the adequacy of the safety database, as described in ¶ 119, below.

90. Defendants Gowen and Soergel conducted a conference call on the same day. During the call, Defendant Gowen discussed the results of the Phase 3 trials, stating in part:

> So, these data also emphasize the strong efficacy of OLINVO comparable to morphine, but also suggest that the OLINVO regimen using 0.35 milligram doses allowed patients to dose themselves to the best balance of efficacy and safety and tolerability.
>
> Another important feature of efficacy is the ability of the physician to use the drug as they are accustomed to using conventional opioids, adjusting the dose freely as they optimize therapy to the individual needs of each patient and this is the way physicians work with opioids and we have deliberately generated data using both PCA and bolus dosing over a broad range in our Phase 2 and 3 trials. Doing so clearly demonstrating the efficacy of OLINVO in comparison to morphine.
>
> * * *
>
> Let's turn now to the safety and tolerability of the product. First we've measured respiratory safety in multiple different ways across five clinical trials and in each case have shown the benefit of OLINVO compared to morphine. Here in our Phase 3 APOLLO trials our key secondary endpoint was respiratory safety burdens, which we measure as the product of the incidents of a respiratory safety event and its average duration.
>
> * * *
>
> This chart shows the frequency of respiratory safety events in the two trials and these are new data that we are showing you today and in this case we not only again see the clear trends but also statistical significance in the 0.35 milligram group in APOLLO-1. These data very consistent with our Phase 2 results in which this was our pre-specified endpoint. So we are consistently seeing a meaningful reduction in respiratory safety measures with the 0.35 meg regimen which in APOLLO-1 was about a 50% reduction, both statistically and highly clinically significant. And we also believe that this level

> of reduction will provide meaningful reductions in the cost of care as well.

91. Defendant Gowen's discussion of the positive efficacy and dosing data from the Phase 3 studies contained material omissions in that her statement failed to disclose that the FDA did not agree with Trevena's proposed dosing or primary endpoint, as discussed in ¶¶ 41, 47, above.

92. Likewise, Defendant Gowen's discussion of positive respiratory safety data from the Phase 3 studies omitted the material fact that the FDA did not agree with Trevena's proposal to evaluate the respiratory safety of oliceridine as compared to morphine, as described in ¶ 72, above.

93. On May 4, 2017, Trevena issued a press release announcing its first quarter 2017 financial results. The press release stated in part:

> "This quarter marked a key milestone for our OLINVO program, with the delivery of robust data that we believe will support our new drug application and demonstrates the potential value of OLINVO for the management of moderate-to-severe acute pain in the hospital," said Maxine Gowen, Ph.D., chief executive officer. "There remains a critical unmet need for patients who require IV opioids to manage pain but are at risk for poor outcomes from opioid-related adverse effects. Our successful Phase 3 data showed not only significant efficacy of OLINVO versus placebo to support approval, but also showed the potential for fewer gastrointestinal and respiratory adverse effects while providing comparable pain relief to a commonly used morphine regimen."
>
> First quarter and recent corporate highlights
>
> **Announced positive top-line results from two Phase 3 pivotal efficacy studies of OLINVOTM (oliceridine injection) for moderate-to-severe pain.** In February, the Company announced positive data from the APOLLO-1 and APOLLO-2 studies of OLINVO in moderate-to severe-acute pain following hard tissue and soft tissue surgeries, respectively. OLINVO demonstrated significant analgesic efficacy compared to placebo in both studies for all three tested dosing regimens. Consistent with Phase 2b

> results, a 0.35 mg dose regimen provided comparable pain relief to a common IV morphine regimen and showed potential to reduce opioid-related adverse effects on multiple measures of respiratory safety and gastrointestinal tolerability.
>
> **OLINVO program remains on track for a new drug application (NDA) submission in 4Q 2017.** As of March 31, 2017, approximately 600 patients have been treated with OLINVO in the ongoing open-label, multi-procedure ATHENA safety study. In addition, the Company has successfully completed a chemistry, manufacturing, and controls Type B pre-NDA meeting with the U.S. Food and Drug Administration (FDA), and all pre-NDA activities remain on track to support an NDA submission to the FDA in the fourth quarter of 2017.

94. The overview of the "positive" top-line results from the Phase 3 efficacy trials, including that the studies demonstrated "significant analgesic efficacy," the positive results of the dosing regimen, as well as the claims of meaningful improvement in respiratory safety compared to morphine also contained material omissions in that the statements failed to disclose that the FDA did not agree with Trevena's proposed primary endpoint, did not agree with Trevena's proposed dosing, and did not agree with Trevena's proposal to evaluate oliceridine's respiratory safety as compared to morphine, as described in ¶¶ 41, 47, 72, above.

95. The description of the ATHENA safety study also omitted the material fact that the FDA had set minimum criteria for the safety database due to concerns about Trevena's proposed dosing regimen, as described in ¶¶ 41, 47, above. The statement also failed to disclose that Trevena had unsuccessfully modified the proposed maximum dosing and dosing instructions on multiple occasions in order to address the adequacy of the safety database, as described in ¶ 119, below.

96. On May 5, 2017, Trevena met privately with the FDA concerning the design of its Phase 3 clinical trials. According to the FDA's later-published description of those communications:

> May 5, 2017 – Advice on Integrated Statistical Analysis Plan (ISAP) for the Integrated Summary of Safety
>
> Agency agreed with the proposed pooling for the ISAP, the planned subgroups for analysis of intrinsic and extrinsic factors, and planned summarization of adverse events.
>
> FDA reiterated the concerns noted at the November 8, 2016, teleconference regarding the assessment of respiratory safety. It was noted that the RSE as described in the ISS statistical plan would be considered exploratory and would not be acceptable for a proposed labeling claim.

97. On July 20, 2017, Trevena announced that Defendant Soergel, its Chief Medical Officer, was resigning.

98. Also, on July 20, 2017, Defendants Gowen and Soergel presented the results of the ATHENA safety study at their 2017 Analyst Day. During the presentation, Defendant Gowen discussed the safety study, stating: "And of course, **we now have a complete safety database to support the NDA file**." During the Q&A portion of the presentation, Defendants Gowen and Soergel answered a question from Antonio Eduardo Arce, an analyst at H.C. Wainwright & Co. LLC as set forth below:

> Q. And then Maxine, just 1 final question related to commercial. It's a bit early yet – you haven't even submitted – but **wondering your thoughts on how you see ultimately the labeled indication coming out? Do you see any kinds of particular restrictions?**
>
> A. [Gowen] No. I don't think we anticipate restrictions. **We anticipate a broad indication statement because we followed the guidance to get that**. And **we're hoping that we've now generated more than enough data to get broad dosing administration guidance**. So restrictions, I can't think of any that we've identified at this point.
>
> A. [Soergel] So **our goal has been to have a label that looks like other opioids from the perspective of lack of a maximum dose, huge flexibility of administration** and then language around titration. **So take care of the patient's pain with as much drug as**

> **you need to and balance their side effects**, in summary as a (inaudible). So that's been our goal and that's been what we've guided the development plan towards.

99. Defendant Gowen and Soergel's above statements contained material omissions in that they failed to disclose that the FDA informed Trevena that it did not agree with the proposed dosing of up to 100 mg daily for the Phase 3 program because Trevena had previously only studied maximum daily doses of 36.8 mg, and informed Trevena that the safety database must include at least 350 patients exposed to the highest intended dose for the longest expected duration of use. As revealed in the Briefing Document on October 9, 2018, Trevena's safety database failed to meet the FDA's minimum requirements despite lowering the proposed maximum daily dose and dosing instructions on multiple occasions in an attempt to address the adequacy of the safety database. Specifically, the highest dose that had at least 350 patients exposed during the first 24 hours was only 27 mg, and the highest dose with the longest actual duration that had at least 350 patients exposed was only 37.2 mg over 35.5 hours, as described in ¶ 119, below. By the time of the July 20, 2017 statements, Defendants Gowen and Soergel knew, or recklessly disregarded, that the safety database did not meet the FDA's minimum requirements. Given the FDA's explicit instructions for the safety database, Defendants had no reasonable basis to believe that Trevena had a "complete safety database" that would support "broad dosing administration guidance" with "a lack of a maximum dose" and "huge flexibility of administration." Indeed, after receiving notification that the FDA had formally rejected Trevena's application, Trevena acknowledged in a press release on November 2, 2018 that the FDA stated that the "submitted safety database is not of adequate size for the proposed dosing." In other words, the FDA's position was not the result of a difference of opinion in interpreting scientific data. Rather, it was the result of Trevena's blatant failure to follow the FDA's explicit instructions.

100. On August 3, 2017, Trevena issued a press release announcing its second quarter 2017 financial results. The press release stated in part:

> "The second quarter saw continued progress towards our goal of delivering an innovative new option for patients who are at risk of adverse events associated with IV opioids like morphine," said Maxine Gowen, Ph.D., chief executive officer. "**We have now completed our Phase 3 clinical development for OLINVO and successfully completed our pre-NDA meetings with the FDA.** In addition, we have refined our commercial strategy to lay the groundwork for a successful commercial launch. **With the comparative data from our successful APOLLO pivotal efficacy studies, as well as data and investigator observations from more real-word use in the ATHENA open label study**, we believe the value of OLINVO will resonate with potential prescribers who want to improve the care of hospital patients suffering severe pain."
>
> Second quarter and recent corporate highlights
>
> OLINVO™ (oliceridine injection) program remains on track for a new drug application (NDA) submission in September/October 2017. **In July 2017, the Company announced that enrollment in the ATHENA open-label safety study was complete to support the NDA file, with 772 patients treated with OLINVO across more than 40 sites.** In addition, the Company successfully completed a chemistry, manufacturing, and controls (CMC) Type B pre-NDA meeting and a preclinical and clinical Type B pre-NDA meeting with the U.S. Food and Drug Administration (FDA). All pre-NDA activities remain on track to support an NDA submission to the FDA in September/October of 2017.

101. The description of the "comparative data from our successful APOLLO pivotal efficacy studies" contained material omissions in that the statement failed to disclose that the FDA did not agree with Trevena's proposed primary endpoint, non-inferiority margin for comparing morphine to oliceridine, as described in ¶¶ 41, 47, above. The statement also omitted the material fact that the FDA disagreed with Trevena's proposal to evaluate the respiratory safety of oliceridine as compared to morphine – a concern that was reiterated to Trevena in May of 2017, as described in ¶¶ 72, 96, above.

102. The statement that the "ATHENA open-label safety study was complete to support the NDA file" also contained material omissions in that it failed to disclose that Trevena had modified the proposed maximum daily dosing and dosing instructions on multiple occasions in order to address the adequacy of the safety database – which required at least 350 patients exposed to the highest intended dose for the longest expected duration of use – and that Trevena was never able to meet this FDA-imposed requirement, as described in ¶¶ 41, 47, above, and ¶ 119, below.

103. On November 7, 2017, Trevena issued a press release announcing its third quarter 2017 financial results. The press release stated in part:

> "The recent submission of the OLINVO NDA capped a transformative period for our Company," said Maxine Gowen, Ph.D., chief executive officer. "We are now focused on preparing for the approval and commercialization of OLINVO, while continuing to advance our development pipeline following our recent strategic decision to halt our discovery research efforts. To this end, new results continue to highlight the potential value of OLINVO for patients in a real world setting who require IV opioids but are at risk of opioid-related adverse events. Positive interim Phase 1 data for TRV250 bode well for future clinical development of this exciting potential migraine therapy."
>
> Third quarter and recent corporate highlights
>
> **OLINVO New Drug Application submitted.** The Company recently submitted its New Drug Application (NDA) for OLINVO to the U.S. Food and Drug Administration (FDA). OLINVO is the first G protein biased ligand of the mu opioid receptor, a new class of opioid receptor modulator, and the first pain program to receive Breakthrough Therapy designation from the FDA. **The submission includes data showing that intravenous OLINVO demonstrated analgesic efficacy in all three dosing regimens tested in the two Phase 3 APOLLO pivotal efficacy studies. These trials were designed to support an indication for the management of moderate-to-severe acute pain in adult patients for whom an intravenous opioid is warranted. The filing also includes safety and tolerability data for over 1,100 patients administered OLINVO across Phase 2 and Phase 3 studies, including the ATHENA open label safety study. Additional pharmacokinetic data, clinical pharmacology data, and results from five**

> **randomized controlled trials with head to head comparisons to morphine, support potential differentiation of OLINVO.**
>
> **New data from Phase 3 ATHENA open label safety study**. In July, the Company announced top-line results from the first 418 patients administered OLINVO to manage medical or postoperative pain in the ATHENA study, which was designed to model real-world use including multimodal analgesia regimens incorporating OLINVO. Data for all 768 patients administered OLINVO are now final, and highlight the effectiveness and utility of OLINVO in treating patients who require an IV opioid to manage pain. . . .

104. The description Trevena provided of its NDA submission concerning efficacy, dosing, and secondary endpoints contained material omissions in that the statement failed to disclose that the FDA disagreed with Trevena's proposed dosing, primary endpoint, and non-inferiority margin for comparing morphine to oliceridine – on which the ability to secure inclusion of secondary endpoints on a potential label depended, as described in ¶¶ 41, 47, above. The statement also omitted the material fact that the FDA disagreed with Trevena's proposal to evaluate the respiratory safety of oliceridine as compared to morphine – a concern that was reiterated to Trevena in May of 2017, as described in ¶¶ 72, 96, above.

105. Trevena's statement that the data for the ATHENA safety study was now complete contained material omissions in that it failed to disclose that Trevena had failed meet the FDA's requirement of providing a safety database that included at least 350 patients exposed to the highest intended dose for the longest expected duration of use, despite modifying the proposed maximum daily dose and dosing instructions on multiple occasions in order to address the adequacy of the safety database, as described in ¶¶ 41, 47, above, and ¶ 119, below.

106. On March 7, 2018, Trevena issued a press release announcing its fourth quarter and fiscal year 2017 financial results. The press release stated in part:

> "**2017 marked important progress for Trevena as we completed our Phase 3 program and NDA submission for OLINVO and prepared to support commercial launch**," said Maxine Gowen, Ph.D., chief executive officer. "**We look forward to potential approval of OLINVO later this year**, as well as advancement of our earlier R&D programs. We remain committed to bringing patients innovative medicines for safer and more successful pain management."
>
> 2017 and recent corporate highlights
>
> **New Drug Application (NDA) for OLINVO submitted and accepted.** In January 2018, the Company announced that the FDA has accepted the Company's NDA for OLINVO. OLINVO is an investigational product for the management of moderate to severe acute pain. It is the first G protein biased ligand of the mu receptor designed to provide IV opioid pain relief with fewer associated adverse effects. The FDA has informed the Company that it intends to convene an advisory committee meeting to discuss the OLINVO NDA ahead of the Prescription Drug User Fee Act (PDUFA) review date of November 2, 2018. If approved, the Company expects commercial launch of OLINVO in the first quarter of 2019 following DEA scheduling.
>
> **Announced top line data from the successful Phase 3 open label ATHENA safety study.** In November, the Company announced top-line results from 768 patients administered OLINVO to manage medical or postoperative pain in the ATHENA study, which was designed to model real-world use including multimodal analgesia regimens incorporating OLINVO. Data highlight the potential effectiveness and utility of OLINVO in treating patients who require an IV opioid to manage acute pain. Patients at elevated risk of opioid-related adverse events were well represented in the study; more than 30% of patients were 65 years or older, and more than 50% of patients were obese, with body mass index (BMI) >30 kg/m2. Only 4% of patients discontinued for lack of efficacy, and 2% of patients discontinued for adverse events. Adverse event rates associated with OLINVO administered by patient controlled analgesia (PCA) and as-needed clinician-administered bolus dosing were similar, supporting potential use of OLINVO in both administration paradigms.

107. The statement concerning the completion of the Phase 3 program and NDA submission contained material omissions in that the statement failed to disclose that the FDA

disagreed with Trevena's proposed dosing, primary endpoint, and non-inferiority margin for comparing morphine to oliceridine – on which the ability to secure inclusion of secondary endpoints on a potential label depended, as described in ¶¶ 41, 47, above. The statement also omitted the material fact that the FDA disagreed with Trevena's proposal to evaluate the respiratory safety of oliceridine as compared to morphine – a concern that was reiterated to Trevena in May of 2017, as described in ¶¶ 72, 96, above. Defendant Gowen's statement that "[w]e look forward to potential approval of OLINVO later this year" was also materially false and misleading because the foregoing omissions concealed the fact that FDA approval for Olinvo was unlikely.

108. The description of the ATHENA safety study also contained material omissions in that it failed to disclose that Trevena had failed meet the FDA's requirement of providing a safety database that included at least 350 patients exposed to the highest intended dose for the longest expected duration of use, despite modifying the proposed maximum daily dose and dosing instructions on multiple occasions in order to address the adequacy of the safety database, as described in ¶¶ 41, 47, above, and ¶ 119, below.

109. On April 6, 2018, Trevena issued a press release announcing that Defendant Gowen would be retiring from the Company effective October 1, 2018.

110. On May 3, 2018, Trevena issued a press release announcing first quarter 2018 financial results. The press release stated in part:

> "In 2018, we have made important progress in Trevena's evolution," said Maxine Gowen, Ph.D., president and chief executive officer. . . . "**We continue to have an ongoing productive dialogue with the FDA as they review our oliceridine NDA, and look forward to an advisory committee meeting later this year and potential approval in November**."
>
> First quarter and recent corporate highlights

> **New Drug Application (NDA) for oliceridine submitted and accepted**. In January 2018, the Company announced that **the FDA has accepted the Company's NDA for oliceridine**, an investigational product for the management of moderate to severe acute pain. Oliceridine is the first G protein biased ligand of the mu receptor, and was designed to provide IV opioid pain relief with fewer associated adverse effects. **The FDA has informed the Company that it intends to convene an advisory committee meeting to discuss the oliceridine NDA ahead of the Prescription Drug User Fee Act (PDUFA) review date of November 2, 2018. If approved, the Company expects commercial launch of oliceridine in the first quarter of 2019, following DEA scheduling.**

111. The positive description of Trevena's dialogue with the FDA and that the Company was "look[ing] forward to an advisory committee meeting later this year and potential approval in November" contained material omissions in that the statement failed to disclose that the FDA disagreed with Trevena's proposed dosing, primary endpoint, and non-inferiority margin for comparing morphine to oliceridine – on which the ability to secure inclusion of secondary endpoints on a potential label depended, as described in ¶¶ 41, 47, above. The statement also omitted the material fact that the FDA disagreed with Trevena's proposal to evaluate the respiratory safety of oliceridine as compared to morphine – a concern that was reiterated to Trevena in May of 2017, as described in ¶¶ 72, 96, above. The omitted information concealed the fact that FDA approval for Olinvo was unlikely.

112. On June 15, 2018, Trevena announced that it had entered into a Sales Agreement with Cowen and Company LLC ("Cowen") pursuant to which it would issue to Cowen and Cowen would sell up to $50 million of Trevena common stock at market prices. Trevena filed a prospectus with the SEC in connection with this anticipated offering that expressly incorporated by reference the Company's 2017 10-K and its first quarter 2018 10-Q, among other filings the Company had

made with the SEC. The prospectus also expressly incorporated by reference all of the filings Trevena made with the SEC until the offering was complete.

113. On August 2, 2018, Trevena issued a press release announcing its second quarter 2018 financial results. The press release stated in part:

> "The second quarter saw important progress towards Trevena's long-term success," said Maxine Gowen, Ph.D., President and Chief Executive Officer. "**We remain confident that the oliceridine NDA remains on track for an FDA decision by the November 2, 2018 PDUFA date, and we look forward to discussing the oliceridine data at an Advisory Committee meeting, likely in October**. . . ."
>
> Second quarter and recent corporate highlights
>
> **Prescription Drug User Fee Act (PDUFA) date for oliceridine**: **November 2, 2018.** Oliceridine is an investigational product under FDA review for the management of moderate to severe acute pain where parenteral opioid analgesia is warranted and was designed to provide the pain relief of IV opioids with fewer associated adverse effects. **The FDA has informed the Company that it intends to convene an advisory committee meeting, likely in October, to discuss the oliceridine NDA. If oliceridine is approved by the FDA, and following DEA scheduling, the Company expects the commercial launch of oliceridine in the first half of 2019**

114. Trevena's statement concerning its NDA submission contained material omissions in that the statement failed to disclose that the FDA disagreed with Trevena's proposed dosing, primary endpoint, and non-inferiority margin for comparing morphine to oliceridine – on which the ability to secure inclusion of secondary endpoints on a potential label depended, as described in ¶¶ 41, 47, above. The statement also omitted the material fact that the FDA disagreed with Trevena's proposal to evaluate the respiratory safety of oliceridine as compared to morphine – a concern that was reiterated to Trevena in May of 2017, as described in ¶¶ 72, 96, above. The statement also failed to disclose that Trevena had failed meet the FDA's requirement of providing a safety database that included at least 350 patients exposed to the highest intended dose for the

longest expected duration of use, despite modifying the proposed maximum daily dose and dosing instructions on multiple occasions in order to address the adequacy of the safety database, as described in ¶¶ 41, 47, above, and ¶ 119, below. The omitted information concealed the fact that FDA approval for Olinvo was unlikely.

THE TRUTH IS REVEALED
THE FDA RELEASES ITS BRIEFING DOCUMENT, REVEALING DEFENDANTS' FRAUD

115. Trevena's fraud was revealed to the market on October 9, 2018. On that day, as is customary, the FDA's Anesthetic and Analgesic Drug Products Advisory Committee publicly issued a Briefing Document in advance of its previously scheduled October 11, 2018 meeting to vote on its recommendation concerning the FDA's approval of Olinvo.

116. This document revealed to the public for the first time the private interactions between the FDA and Trevena described in ¶¶ 33-37, 41, 47, 51, 72, 96, above.

117. The briefing document made clear that the FDA's previously issued concerns were not heeded by Trevena. The market immediately understood that the committee was not recommending the approval of Olinvo.

118. Specifically, the briefing document stated:

> Efficacy: In FDA's analysis of efficacy for Study 3001, all three doses of oliceridine (0.1 mg, 0.35 mg, and 0.5 mg) demonstrated a statistically greater reduction in pain intensity than placebo. However, morphine demonstrated a greater reduction in pain intensity than all three doses of oliceridine that was also statistically significant. In FDA's analysis for Study 3002, two of the three doses of oliceridine (0.35 mg and 0.5 mg) demonstrated a statistically greater reduction in pain intensity than placebo, but the 0.1 mg dose did not. In Study 3002, morphine demonstrated a greater reduction in pain intensity relief than two of the doses of oliceridine (0.1 mg and 0.35 mg) that was statistically significant. The reduction in pain intensity by morphine was not greater than that of the highest oliceridine dose (0.5 mg). Currently, Trevena is only seeking approval of the 0.1 mg and 0.35 mg doses.

> A secondary objective of the studies was to demonstrate the superiority of oliceridine to morphine in terms of respiratory safety burden. ***FDA did not agree with Trevena's proposed endpoint due to concerns with its clinical meaningfulness***. Further, when evaluating this endpoint in both studies, none of the oliceridine treatment arms demonstrated a significant reduction in the expected cumulative duration of respiratory safety events compared to morphine. ***Further, any numeric trends in terms of respiratory safety must be considered in the context of the observed efficacy. A conclusion of benefit in a dose-related safety outcome cannot be made without a demonstration of similar efficacy***.
>
> Safety: Opioids are typically administered as needed (PRN) for acute pain. In the Phase 3 studies, the oliceridine dosing regimen included a clinician-administered loading dose, patient-delivered PRN dosing via patient-controlled analgesia (PCA) pump, clinician-administered PRN supplemental dosing, or some combination of these. ***This complex PRN dosing resulted in a wide range of patient exposures and added complexity to the safety analyses.*** Given the variability in doses administered, the Applicant and Agency analyzed safety in a variety of ways, including by randomized treatment regimen and by cumulative oliceridine exposure.
>
> The agency analysis of the safety of oliceridine in the Phase 3, double-blind studies focused on comparisons of the randomized oliceridine treatment arms by study, so that the safety results could be considered in the context of the efficacy of the evaluated doses. Many adverse events in the clinical program were consistent with opioid-related adverse events, including respiratory depression and hypoxia, and nausea and vomiting. When evaluating the controlled Phase 3 data by randomized treatment group, many of the adverse events were dose-related, including respiratory effects. While there were trends showing a decreased percentage of respiratory events as defined by the applicant with oliceridine than morphine for some parameters, this was not consistent across all parameters. ***Notable safety issues in the clinical program included hepatic adverse events and QT prolongation. An additional consideration is whether the safety database is adequate to support the proposed dosing.***

119. The briefing document also contained a plethora of information demonstrating that Trevena failed to heed the FDA's advice throughout the review process. These issues were concealed from investors, and the market, and contributed significantly to the ultimate vote against

approval for Olinvo. The table below lists the issues raised by the FDA during the review process in the left column, and summarizes the impact of Trevena's failure to address those issues in the right column:

Regulatory Interaction	Discussion in Briefing Document
March 3, 2016 – Advice regarding ECGs – Written Advice FDA issued written advice to the Applicant because QTcF prolongation exceeded the 10-ms regulatory threshold at clinically relevant exposures. The Applicant was instructed to submit amendments to modify all protocols for ongoing clinical trials to include the following safety assessments, and incorporate them into any future clinical trials: 1. Conduct safety ECG monitoring at baseline, following the first dose, and periodically thereafter. The timing of ECGs will need to reflect the delayed response relative to time of peak concentrations that was observed in the thorough QT study. Include additional ECG monitoring until ECGs return to baseline in patients discontinued from the trial or requiring dose reduction due to QTc interval prolongation. 2. Periodic monitoring of electrolytes (subjects already participating in the study with serum potassium, magnesium, or calcium levels outside of the central laboratory's reference range should be carefully monitored and brought to normal values). 3. Propose dose-modification and discontinuation criteria in subjects with posttreatment QTc > 500 ms or post-baseline increases > 60 ms.	Because the QTcF prolongation exceeded the 10-ms regulatory threshold at clinically relevant exposures, **FDA sent an advice letter/information request to the Applicant** on 3/3/16, indicating that the Applicant should incorporate safety ECG monitoring at baseline, following the first dose, and periodically thereafter. **It was noted that the timing of the ECGs will need to reflect** that delayed response relative to peak concentrations that was observed in the thorough QT study. In the Applicant's Phase 3 studies, **only limited ECG monitoring was obtained** in patients (1, 24, and 48-hours post-loading doses for study 3001 and 1 and 24 hours for Study 3002). Given that QTcF prolongation associated with oliceridine is delayed and oliceridine is administered as needed with a wide range of doses up to a proposed maximum daily dose of initially 100mg and then deceased by the Applicant to 40mg, the data from a single dose tQT study and **the limited ECG monitoring data obtained in Phase 3 do not appear to be adequate to evaluate the QT effects of oliceridine.** While the Applicant states that there were no significant QTcF changes noted in the clinical studies, studies 3001, 3002, or 3003 were not designed to characterize the QT prolonging effect of oliceridine" and "Further, it is worth noting that the ECG monitoring was sparse (baseline, 1 hour, and every 24 hours) and the absence of observed QTc prolongation **is therefore not particularly reassuring.** The concerns regarding QT prolongation were noted by the Agency at the Midcycle

	Communication with the Applicant on May 21, 2018. In follow-up, the Applicant proposed simulations of the QTcF under various dosing scenarios a re-analysis of the tQT study using different ECG biomarkers. The Agency responded that since mechanism of the delayed QTcF prolongation is unknown, **it is not appropriate to extrapolate information** from single 3 mg and 6 mg does to the proposed multiple dose scenarios (up to 3 mg every 1 hour).
March 29, 2016 (meeting minutes April 28, 2016) – End-of-Phase 2 Meeting FDA did not agree with the proposed dosing in the Phase 3 studies. The Sponsor proposed dosing up to 100 mg daily (including a 0.75 mg every 1 hour as needed clinician administered dose), but had only studied maximum daily doses of 36.8 mg. Further, the Sponsor did not have adequate non-clinical support for the proposed doses. FDA noted that the safety database must include at least 350 patients exposed to the highest intended dose for the longest expected duration of use. It was noted that the safety database requirements might change if safety signals arise during development that require further evaluation.	A **significant consideration during the review cycle was whether the size of the safety database was adequate**. Prior to submission of the NDA, **the Applicant was told at the End-of-Phase 2 meeting and the pre-NDA meeting that they would need at least 350 patients exposed to the highest intended doses for the longest expected duration of use.** Figure 15 shows the frequency of cumulative exposure to oliceridine for the first 24 hours for the pooled Phase 2 and Phase 3 studies. **The data are skewed**, with most patients receiving doses less than 75 mg. The Applicant's initially proposed labeling included a maximum daily dose of 100 mg without a limit on duration of use. The Applicant was asked to clarify the highest does that has at least 350 patients exposed for 24 hours and the highest does that has at least 350 patients exposed for the longest actual duration of use. The highest dose that has at least 350 patients exposed during the first 24 hours of dosing was 27 mg of oliceridine. The highest dose with the longest actual duration that has at least 350 patients exposed was 37.2 mg of oliceridine over an actual duration of at least 35.5 hours. During the review cycle, the **Applicant reduced the proposed maximum daily dose** from 100 mg daily to 40 mg daily **to try to address the adequacy of the safety database and nonclinical concerns regarding the adequacy to qualify major metabolites**. During the review cycle, **Trevena modified the recommended maximum daily dose and**

	dosing instruction in the proposed label several times.
March 29, 2016 (meeting minutes April 28, 2016) – End-of-Phase 2 Meeting FDA did not agree with the proposed primary endpoint, as it was unclear how a 30% improvement from baseline based on SPID correlates to an improvement in pain intensity scores on the NRS in the proposed setting of acute postoperative pain and if that change is clinically relevant. The Applicant provided details of a proposed approach to missing data. This approach included replacing pain scores in the window determined dosing interval described in the label of the rescue medication following rescue with the pain score recorded immediately prior to rescue	This **endpoint is novel and has never been the basis for approval for any drugs in this class**. **Consequently, sensitivity analyses were also performed directly on the SPID scores** which are typically used as the primary efficacy endpoint in this setting. Since the Applicant's primary efficacy analyses was based on a novel responder definition, i.e. 30% improvement in SPIDs, FDA conducted an analysis using SPIDs rather than the proposed responder definition. **FDA disagreed with how information regarding use of rescue medication was used in the Applicant's derivation of SPIDs.** Carrying forward the final pre-rescue score from the first use of rescue until the end of the observation period ignores the fact that the effect of the rescue medication will expire, and the fact that patient's pain scores would continue to improve throughout the study even in the placebo arm. **The consequence is that it harshly penalizes patients who used rescue medication. FDA used an alternative analysis which carries forward the pre-rescue scores for the dosing interval of the rescue medication, which is commonly used in studies of analgesics in the post-surgical setting, and considered the most clinically relevant**.
March 29, 2016 (meeting minutes April 28, 2016) – End-of-Phase 2 Meeting FDA did not agree with the proposed non-inferiority (NI) margin for comparing morphine to oliceridine.	Secondary Efficacy Analysis: -Non-inferiority assessment of oliceridine to morphine: **While this is critical in light of the application's objective of demonstrating a reduction in the respiratory safety burden for oliceridine compared to morphine, there was no agreement on the Applicant's definition of the non-inferiority criteria**.
March 29, 2016 (meeting minutes April 28, 2016) – End-of-Phase 2 Meeting Any comparative safety claims must be replicated, adequately justified for clinical relevance, and established in the setting of	A secondary objective of the studies was to demonstrate the superiority of oliceridine to morphine in terms of respiratory safety burden. **FDA did not agree with Trevena's proposed endpoint due to concerns with its clinical meaningfulness**. Further, when

comparable efficacy between comparators to be considered for inclusion in labeling	evaluating this endpoint in both studies**, none of the oliceridine treatment arms demonstrated a significant reduction** in the expected cumulative duration of respiratory safety events **compared to morphine**. Further, any numeric trends in terms of respiratory safety events must be considered in the context of the observed efficacy. A **conclusion of benefit in a dose-related safety outcome cannot be made without a demonstration of similar efficacy**.
November 8, 2016 (meeting minutes 12/19/16) – Type C teleconference FDA did not agree with Trevena's proposal to evaluate the respiratory safety of oliceridine as compared to morphine because the definition of Respiratory Safety Events (RSEs) was not clearly defined and the determination of the presence of an RSE relied largely on clinical acumen. Even though the parameters proposed in the evaluation of an RSE (respiratory rate, oxygen saturation, and MRPSS somnolence/sedation scores) are well accepted criteria used for the assessment of patients at risk for experiencing an RSE, it is unclear that a small change in these parameters is of clinical significance. Trevena was told to specify a clinically meaningful definition of an RSE, such as patients who require a clinical intervention after meeting a specific criterion (e.g., naloxone administration and/or oxygen administration with a reduction in oxygen saturation). Further, FDA did not agree with inclusion of sedation and somnolence in the RSE definition. FDA stated that the statistical model proposed to evaluate the respiratory safety of oliceridine incorporates both the population prevalence of RSEs and the population conditional mean cumulative duration of RSEs to describe respiratory safety burden (RSB). Based on this model, a small change in event duration could result in a statistically significant result without clinical significance. In addition, the RSB endpoint is difficult to interpret and apply	**The key secondary safety endpoint** was the respiratory safety burden, as measured by the occurrence and duration of respiratory safety events (RSEs) within patients. The Applicant also recorded information on the cumulative duration of supplemental oxygen administration and the cumulative duration of recovery from RSE. A RSE was defined as a clinically relevant worsening of respiratory status. The respiratory safety burden safety/tolerability endpoint incorporated both the prevalence of RSEs and the expected duration of time that a patient would experience an RSE if one occurred, into a single composite measure. This endpoint was intended to correspond to the total amount of time a patient from the population should have expected to experience an RSE and represents the respiratory safety burden for a given treatment regimen. **However, there is no precedent for use of this endpoint in a clinical study and the FDA did not agree that this was a clinically interpretable endpoint for the evaluation of a potential respiratory claim. During development, FDA informed the Applicant that their definition of RSE was not clearly defined and relied largely on clinical acumen.** Based on oliceridine's mechanism of action, the Applicant hypothesized that it may be

directly to clinical practice. Trevena was asked to analyze and report event duration separately from the event prevalence & **May 5, 2017 – Advice on Integrated Statistical Analysis Plan (ISAP) for the Integrated Summary of Safety** Agency agreed with the proposed pooling for the ISAP, the planned subgroups for analysis of intrinsic and extrinsic factors, and planned summarization of adverse events FDA reiterated the concerns noted at the November 8, 2016, teleconference regarding the assessment of respiratory safety. It was noted that the RSE as described in the ISS statistical plan would be considered exploratory and would not be acceptable for a proposed labeling claim	associated with less respiratory depression than other opioids. The Applicant pre-specified a safety endpoint referred to as respiratory safety burden to assess the respiratory safety of oliceridine compared to morphine and placebo. However, FDA did not agree with the Applicant's proposal to evaluate respiratory safety based on respiratory safety events (RSEs) or respiratory safety burden as discussed in Section 1.1. **A significant Agency concern was whether the Applicant's definition of an RSE or a small change in RSE was clinically meaningful**. Of note, the Applicant performed study 1003, which assessed ventilatory response to hypercapnia and cold pain testing in healthy volunteers. **The Agency considers this study to be a proof-of-concept study that is not adequate to provide regulatory support for a respiratory safety claim**.

120. Upon publication of this news, Trevena common stock plummeted. Shares closed on October 9, 2018 down 64% from the prior trading day with unusually high volume—more than 40 million shares traded hands.

121. Investors knew the Advisory Committee's recommendation would be important to the FDA: In an article published August 16, 2016 on the website www.eyeonfda.com, titled *AdComm Recommendations – How Often FDA Does Not Follow Them?*, attorney and pharmaceutical industry consultant Mark Senak analyzed every advisory committee meeting held from 2011 through 2016. Of the 231 meetings, 145 were held to consider a treatment candidate for approval – with a decision reached in 136 of those 145 meetings. Of the 136 meetings, the FDA went against the recommendation of the Advisory Committee on just 13 occasions, or less than

10% of the time. In other words, the FDA nearly always follows the recommendation of the Advisory Committee.[5]

122. On October 11, 2018, Trevena filed with the SEC a Current Report on Form 8-K, pursuant to Regulation F-D, concerning some of the Company's prior communications with the FDA about its Phase III clinical trial design for Olinvo:

> Trevena, Inc. (the "Company" or the "Sponsor") is providing the following information to clarify and further expand upon the interactions between Trevena and the U.S. Food and Drug Administration ("FDA") with respect to the primary endpoint for the two pivotal Phase 3 studies, APOLLO-1 and APOLLO-2, conducted by the Company with respect to oliceridine.
>
> ***Prior to the Company's End-of-Phase 2 meeting, the Division of Anesthesia, Analgesia, and Addiction Products (the "Division"), Center for Drug Evaluation and Research of FDA indicated to the Company that it did not agree with the proposed primary efficacy endpoint for the APOLLO-1 and APOLLO-2 studies. Following this, the Company submitted additional analyses to, and had further discussions with, the Division.*** In the meeting minutes dated April 28, 2016 from the End-of-Phase 2 meeting between the Division and the Company, the Division indicated the following to the Company:
>
> "Regarding the relevance of the proposed primary endpoint, the Sponsor plans to include multiple secondary endpoints in their analyses to reflect appropriate endpoints of clinical importance. They have tried patient global assessments, but these have limitations in the acute setting. The Division stated that while a 30% improvement in summed pain intensity difference (SPID) is acceptable statistically, ***the clinical relevance of a 30% improvement in this setting using this measure is not clear***. Interpretability of SPIDs can be challenging because ***the value is dependent on the formula for calculating the SPID and has no obvious meaning***. Further, the SPID may be different for the two treatment groups, but the difference can reflect only an early or late effect. The Division stated that a 30% decrease in pain has typically been used as a marker to determine a clinically-meaningful

[5] *See also,* Michael Becker, *Warning Biotech Investors: FDA Advisory Panels' No Means No, Yes Means Maybe*, SEEKING ALPHA (Feb. 7, 2011, 12:59 PM) https://seekingalpha.com/article/251267-warning-biotech-investors-fda-advisory-panels-no-means-no-yes-means-maybe (finding that from 2010 through 2011, the FDA agreed with the advisory committee in all nine instances where the committee made negative recommendations).

> difference in chronic pain settings. The Division has no objection to use of a responder rate as an endpoint, however, the Sponsor must incorporate those patients who discontinue into the analysis as non-responders." (emphasis added).

123. The Company announced later in the day on October 11, 2018, that the Analgesic Drug Products Advisory Committee of the FDA voted "8 against, and 7 in favor of, the approval of oliceridine for the management of moderate to severe acute pain in adult patients for whom an intravenous (IV) opioid is warranted." The Company acknowledged that while "[t]he FDA [was] not bound by the Advisory Committee's recommendations," it "takes its advice into consideration when making its decision."

124. Trevena stock was halted throughout the day on October 11, 2018, pending news. When trading commenced on October 12, 2018, Trevena stock dropped another 7%, closing below $1 per share, on high volume.

125. On November 2, 2018, Trevena disclosed that the FDA had formally rejected its NDA for Olinvo, stating in a Complete Response Letter[6] that, among other things, Trevena's safety database was not adequate for the proposed dosing and that additional clinical data on QT prolongation was required. While Trevena did not disclose the full contents of the Complete Response Letter, which remains confidential, the two reasons for rejection that Trevena did disclose were raised by the FDA prior to the start of the Phase 3 trials, as described in ¶¶ 33, 41, 47, above.

[6] A Complete Response Letter is sent by the FDA to an applicant "to indicate that the review cycle for an application is complete and that the application is not ready for approval." *See* https://www.fda.gov/drugs/laws-acts-and-rules/complete-response-letter-final-rule.

CLASS ACTION ALLEGATIONS

126. Lead Plaintiffs bring this action as a class action pursuant to Federal Rules of Civil Procedure 23(a) and 23(b)(3), on behalf of a class consisting of all purchasers of the common stock of Trevena during the Class Period (the "Class"). Excluded from the Class are Defendants, the officers and directors of the Company, at all relevant times, members of their immediate families and their legal representatives, heirs, successors, or assigns, and any entity in which Defendants have or had a controlling interest.

127. The members of the Class are so numerous that joinder of them is impracticable. Throughout the Class Period, Trevena traded on the NASDAQ exchange. While the exact number of class members is not presently known to Lead Plaintiffs, and can only be ascertained through discovery, Lead Plaintiffs believe there are thousands of members in the proposed Class. Record owners and other members of the Class can be ascertained through records maintained by Trevena and/or its transfer agent. Those record holders could be notified of the pendency of this action by mail.

128. Lead Plaintiffs' claims are typical of the claims of the members of the Class, as all are similarly affected by Defendants' wrongful conduct in violation of federal law.

129. Lead Plaintiffs will fairly and adequately protect the interests of the members of the class and have retained competent and experienced securities litigation counsel.

130. Common questions of law and fact exist as to all members of the Class and will predominate over any questions solely affecting individual members of the Class. Among the common questions of law and fact common to the Class:

A. Whether the Exchange Act was violated by Defendants as alleged herein;

B. Whether statements made by Defendants misrepresented and omitted material facts about Trevena's business, operations, and management; and

C. To what extent the members of the Class have suffered damages, and the proper measure of those damages.

131. A class action is superior to all other available methods for the fair and efficient adjudication of this controversy, given that joinder of all members is impracticable. As the damages suffered by each individual Class member may be relatively small, the burden and expense of litigating individual cases would make it all but impossible for many members of the Class to redress wrongs done to them. There will not be any difficulty in managing this action as a class action.

FRAUD ON THE MARKET

132. Lead Plaintiffs will reply upon the presumption of reliance established by the fraud-on-the-market doctrine. Among other things:

a. Defendants made public misrepresentations or failed to disclose material facts during the Class Period;

b. These omissions and material misrepresentations were material;

c. Trevena common stock traded in an efficient market throughout the Class Period;

d. The misrepresentations alleged would tend to induce a reasonable investor to misjudge the value of Trevena common stock; and

e. Lead Plaintiffs and other members of the Class purchased Trevena common stock between the time Defendants misrepresented or failed to disclose material facts and the time the true facts were disclosed, without knowledge of the misrepresented or omitted facts.

133. At all relevant time, the market for Trevena common stock was efficient, as:

a. Trevena filed periodic public reports with the SEC as a regulated issuer; and

b. Trevena regularly communicated with public investors via established communications mechanisms, including through the regular dissemination of press releases on major news wire services, communications through the financial press, securities analysts, the internet, and other similar reporting services.

NO SAFE HARBOR

134. So-called Safe Harbor Warnings that accompanied Trevena's purportedly forward-looking statements ("FLS") issued during the Class Period were ineffective to shield those statements from liability.

135. Projected revenues and earnings that were included in Trevena's financial reports, to the extent they were prepared in accordance with Generally Accepted Accounting Principles ("GAAP"), including those filed with the Securities Exchange Commission, are excluded from the protection of the statutory Safe Harbor. 15 U.S.C. § 78u-5(b)(2)(A).

136. Defendants are also liable for any false or misleading FLS pleaded because, at the time each FLS was made, the speaker knew it was false or misleading and the statement was authorized or approved by an executive officer of Trevena who knew that the statement was false. None of the historic or present tense statements made by Defendants were assumptions underlying or relating to any plan, projection, or statement of future economic performance, as they were not stated to be such assumptions underlying or relating to any projection or statement of future economic performance when made. None of the projections or forecasts made by Defendants expressly related to or were stated to be dependent on historic or present tense statements when made.

LOSS CAUSATION AND ECONOMIC LOSS

137. During the Class Period, as detailed herein, Defendants made false and misleading statements and engaged in a scheme to deceive the market, thereby artificially inflating the price

of Trevena common stock. This operated as a fraud or deceit on Class Period purchasers of Trevena common stock by misrepresenting the true value of the Company's business and financial prospects. When Defendants' misrepresentations and fraudulent conduct became apparent to the market, Trevena common stock fell precipitously, as the prior artificial inflation came out of the price.

138. Trevena shares fell more than 64% on October 9, 2018, immediately after and as a result of the news described in ¶¶ 115-120, which corrected the materially false statements and omissions alleged above.

139. Trevena shares fell another 7% on October 12, 2018, immediately after and as a result of the news described in ¶¶ 122-124, which further corrected the materially false statements and omissions alleged above.

140. As a result of their purchase of Trevena common stock during the Class Period, Plaintiffs and other members of the Class suffered economic loss—*i.e.*, damages—under the federal securities laws.

CAUSES OF ACTION

COUNT ONE
VIOLATIONS OF SECTION 10(B) OF THE EXCHANGE ACT AND RULE 10B-5 (AGAINST ALL DEFENDANTS)

141. Lead Plaintiffs incorporate the above numbered paragraphs by reference.

142. During the Class Period, Defendants disseminated or approved the false statements specified above, which they knew or deliberately disregarded were misleading in that they contained misrepresentations, and failed to disclose material facts necessary in order to make the statements made, in light of the circumstances under which they were made, not misleading.

143. Defendants violated Section 10(b) of the Exchange Act and Rule 10b-5 in that they: (a) employed devices, schemes, and artifices to defraud; (b) made untrue statements of material

facts and omitted to state material facts necessary in order to make statements made, in light of the circumstances under which they were made, not misleading; or (c) engaged in acts, practices, and a course of business that operated as a fraud or deceit upon Lead Plaintiffs and others similarly situated in connection with their purchases of Trevena common stock during the Class Period.

144. Lead Plaintiffs, and the Class, have suffered damages in that, in reliance on the integrity of the market price, they paid artificially inflated prices for Trevena common stock. Lead Plaintiffs and the Class would not have purchased Trevena common stock at the prices they paid, or at all, if they had been aware that the market prices had been artificially and falsely inflated by Defendants' misleading statements.

COUNT TWO
VIOLATIONS OF SECTION 20(A) OF THE EXCHANGE ACT
(AGAINST THE INDIVIDUAL DEFENDANTS)

145. Lead Plaintiffs incorporate the above numbered paragraphs by reference.

146. The Individual Defendants acted as control persons of Trevena within the meaning of Section 20(a) of the Exchange Act as alleged herein. By virtue of their intimate knowledge of the false and misleading statements made during the Class Period, they had the power to influence and control, and did influence and control, directly or indirectly, the decision-making of Trevena, including the content and dissemination of the false and misleading statements alleged herein.

147. The Individual Defendants were provided with or had unlimited access to copies of the statements alleged to be misleading prior to and/or shortly after those statements were issued, and had the ability to prevent the issuance of those statements or to cause those statements to be corrected.

148. As set forth above, the Individual Defendants had the ability to exercise control over, and did control, Trevena, which violated Section 10(b) of the Exchange Act and Rule 10b-5

promulgated thereunder, in connection with the false and materially misleading statements alleged herein.

149. By virtue of these facts, the Individual Defendants have violated Section 20(a) of the Exchange Act, and are liable to Plaintiff and the other members of the Class.

PRAYER FOR RELIEF

WHEREFORE, Lead Plaintiffs pray for relief and judgment as follows:

A. Determining that this action is a proper class action, and certifying Lead Plaintiffs as Class representatives under Rule 23 of the Federal Rules of Civil Procedure and Lead Plaintiffs' counsel as Lead and Local counsel;

B. Awarding compensatory damages in favor of Lead Plaintiffs and the other Class members against all Defendants, jointly and severally, for all damages sustained as a result of Defendants' wrongdoing, in an amount to be proven at trial, including interest thereon;

C. Awarding Lead Plaintiffs and the Class their reasonable costs and expenses incurred in this action, including counsel fees and expert fees;

D. Awarding rescission or rescissory damages; and

E. Awarding such equitable or injunctive relief or other relief as deemed appropriate by the Court.

JURY DEMAND

Lead Plaintiffs demand a trial by jury.

August 2, 2019

Respectfully submitted,

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